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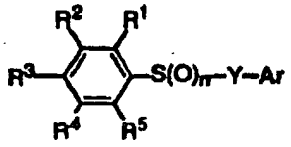
(54) Title: SUBSTITUTED BENZENE COMPOUNDS AS ANTIPROLIFERATIVE AND CHOLESTEROL LOWERING AGENTS

(57) Abstract

The invention provides compounds, compositions and methods relating to novel electrophilic aromatic derivatives and their use as pharmacologically active agents. The compositions find particular use as pharmacological agents in the treatment of disease states, particularly cancer, psoriasis, vascular restenosis, infections, atherosclerosis and hypercholesterolemia, or as lead compounds for the development of such agents. The compositions include compounds of general Formula (I).



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Substituted Benzene Compounds as Antiproliferative and Cholesterol Lowering Agents

INTRODUCTION

Field of the Invention

The field of the invention is substituted benzene derivatives and analogs and their use as pharmacologically active agents capable of lowering plasma cholesterol levels and inhibiting abnormal cell proliferation.

Background

Atherosclerosis is a leading cause of death in the United States. The disease results from excess cholesterol accumulation in the arterial walls, which forms plaques that inhibit blood flow and promote clot formation, ultimately causing heart attacks, stroke and claudication. A principal source of these cholesterol deposits is the low-density lipoprotein (LDL) particles that are present in the blood. There is a direct correlation between LDL concentration and plaque formation in the arteries. LDL concentration is itself largely regulated by the supply of active LDL cell surface receptors, which bind LDL particles and translocate them from the blood into the cell's interior. Accordingly, the upregulation of LDL receptor expression provides an important therapeutic target.

Lipoprotein disorders have been previously called the hyperlipoproteinemias and defined as the elevation of a lipoprotein level above normal. The hyperlipoproteinemias result in elevations of cholesterol, triglycerides or both, and are clinically important because of their contribution to atherosclerotic diseases and pancreatitis.

Lipoproteins are spherical macromolecular complexes of lipid and protein. The lipid constituents of lipoproteins are esterified and unesterified (free) cholesterol, triglycerides, and phospholipids. Lipoproteins transport cholesterol and triglycerides from sites of absorption and synthesis to sites of utilization. Cholesteryl esters and triglycerides are nonpolar and constitute the hydrophobic core of lipoproteins in varying proportions. The lipoprotein surface coat contains the polar constituents - free cholesterol, phospholipids, and apolipoproteins - that permit these particles to be miscible in plasma.

Cholesterol is used for the synthesis of bile acids in the liver, the manufacture and repair of cell membranes, and the synthesis of steroid hormones. There are both exogenous and

endogenous sources of cholesterol. The average American consumes about 450 mg of cholesterol each day and produces an additional 500 to 1,000 mg in the liver and other tissues. Another source is the 500 to 1,000 mg of biliary cholesterol that is secreted into the intestine daily; about 50 percent is reabsorbed (enterohepatic circulation). The rate-limiting enzyme in endogenous cholesterol synthesis is 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. Triglycerides, which are nonpolar lipids consisting of a glycerol backbone and three fatty acids of varying length and degrees of saturation, are used for storage in adipose tissue and for energy.

Lipoproteins are classified into groups based upon size, density, electrophoretic mobility, and lipid and protein composition. Very low density lipoproteins (VLDL) are large, triglyceride-rich lipoproteins that are synthesized and secreted by hepatocytes. VLDL interacts with lipoprotein lipase in capillary endothelium, and the core triglycerides are hydrolyzed to provide fatty acids to adipose and muscle tissue. About half of the catabolized VLDL particles are taken up by hepatic LDL receptors and the other half remain in plasma, becoming intermediate-density lipoprotein (IDL). IDL is enriched in cholesteryl esters relative to triglycerides and is gradually converted by hepatic triglyceride lipase to the smaller, denser, cholesterol ester-rich LDL. As IDL is converted to LDL, apolipoprotein E becomes detached, and only one apolipoprotein remains, apo B-100.

LDL normally carries about 75 percent of the circulating cholesterol. Cellular LDL uptake is mediated by a glycoprotein receptor molecule that binds to apo B-100. Approximately 70 percent of LDL is cleared by receptor uptake, and the remainder is removed by a scavenger cell pathway using nonreceptor mechanisms. The LDL receptors span the thickness of the cell's plasma membrane and are clustered in specialized regions where the cell membrane is indented to form craters called coated pits. These pits invaginate to form coated vesicles, where LDL is separated from the receptor and delivered to a lysosome so that digestive enzymes can expose the cholesteryl ester and cleave the ester bond to form free cholesterol. The receptor is recycled to the cell surface.

As free cholesterol liberated from LDL accumulates within cells, there are three important metabolic consequences. First, there is a decrease in the synthesis of HMG-CoA reductase, the enzyme that controls the rate of *de novo* cholesterol biosynthesis by the cell. Second,

there is activation of the enzyme acyl cholesterol acyltransferase (ACAT), which esterifies free cholesterol into cholesterol ester, the cell's storage form of cholesterol. Third, accumulation of cholesterol suppresses the cell's synthesis of new LDL receptors. This feedback mechanism reduces the cell's uptake of LDL from the circulation.

Lipoproteins play a central role in atherosclerosis. This association with the most common cause of death in the developed world defines the principal clinical importance of the hyperlipoproteinemias. Individuals with an elevated cholesterol level are at higher risk for atherosclerosis. Multiple lines of evidence, including epidemiological, autopsy, animal studies and clinical trials, have established that LDL is atherosclerogenic and that the higher the LDL level, the greater the risk of atherosclerosis and its clinical manifestations. A certain degree of LDL elevation appears to be a necessary factor in the development of atherosclerosis, although the process is modified by many other factors (e.g., blood pressure, tobacco use, blood glucose level, antioxidant level, and clotting factors). Acute pancreatitis is another major clinical manifestation of dyslipoproteinemia. It is associated with chylomicronemia and elevated VLDL levels. Most patients with acute pancreatitis have triglyceride levels above 2,000 mg/dL, but a 1983 NIH consensus development conference recommended that prophylactic treatment of hypertriglyceridemia should begin when fasting levels exceed 500 mg/dL. The mechanism by which chylomicronemia and elevated VLDL levels cause pancreatitis is unclear. Pancreatic lipase may act on triglycerides in pancreatic capillaries, resulting in the formation of toxic fatty acids that cause inflammation.

Abundant evidence indicates that treatment of hyperlipoproteinemia will diminish or prevent atherosclerotic complications. In addition to a diet that maintains a normal body weight and minimizes concentrations of lipids in plasma, therapeutic agents that lower plasma concentrations of lipoproteins, either by diminishing the production of lipoproteins or by enhancing the efficiency of their removal from plasma, are clinically important.

The most promising class of drugs currently available for the treatment of hyperlipoproteinemia or hypercholesterolemia acts by inhibiting HMG-CoA reductase, the rate-limiting enzyme in endogenous cholesterol synthesis. Drugs of this class competitively inhibit the activity of the enzyme. Eventually, this inhibition leads to a decrease in the

endogenous synthesis of cholesterol and by normal homeostatic mechanisms, plasma cholesterol is taken up by LDL receptors to restore the intracellular cholesterol balance.

Through both the release of precursors of LDL and receptor-mediated LDL uptake from the serum, liver cells play a critical role in maintaining serum cholesterol homeostasis. In both man and animal models, an inverse correlation appears to exist between liver LDL receptor expression levels and LDL-associated serum cholesterol levels. In general, higher hepatocyte LDL receptor numbers result in lower LDL-associated serum cholesterol levels. Cholesterol released into hepatocytes can be stored as cholesteryl esters, converted into bile acids and released into the bile duct, or it can enter into an oxycholesterol pool. It is this oxycholesterol pool that is believed to be involved in end product repression of both the genes of the LDL receptor and enzymes involved in the cholesterol synthetic pathway.

Transcription of the LDL receptor gene is known to be repressed when cells have an excess supply of cholesterol, probably in the form of oxycholesterol. A DNA sequence in the LDL receptor promoter region, known as the sterol response element (SRE), appears to confer this sterol end product repression. This element has been extensively investigated (Brown, Goldstein and Russell, U.S. Patents 4,745,060 and 4,935,363). The SRE can be inserted into genes that normally do not respond to cholesterol, conferring sterol end product repression of the chimeric gene. The exact mechanism of the repression is not understood. Brown and Goldstein have disclosed methods for employing the SRE in a screen for drugs capable of stimulating cells to synthesize LDL receptors (U.S. Patent 4,935,363). It would be most desirable if the synthesis of LDL receptors could be upregulated at the level of gene expression. The upregulation of LDL receptor synthesis at this level offers the promise of resetting the level of serum cholesterol at a lower, and clinically more desirable, level. Presently, however, there are no cholesterol lowering drugs that are known to operate at the level of gene expression. The present invention describes methods and compounds that act to inhibit directly or indirectly the repression of the LDL receptor gene, resulting in induction of the LDL receptor on the surface of liver cells, facilitating LDL uptake, bile acid synthesis and secretion to remove cholesterol metabolites and hence the lowering of LDL-associated serum cholesterol levels.

A number of human diseases stem from processes of uncontrolled or abnormal cellular proliferation. Most prevalent among these is cancer, a generic name for a wide range of cellular malignancies characterized by unregulated growth, lack of differentiation, and the ability to invade local tissues and metastasize. These neoplastic malignancies affect, with various degrees of prevalence, every tissue and organ in the body. A multitude of therapeutic agents have been developed over the past few decades for the treatment of various types of cancer. The most commonly used types of anticancer agents include: DNA-alkylating agents (e.g., cyclophosphamide, ifosfamide), antimetabolites (e.g., methotrexate, a folate antagonist, and 5-fluorouracil, a pyrimidine antagonist), microtubule disruptors (e.g., vincristine, vinblastine, paclitaxel), DNA intercalators (e.g., doxorubicin, daunomycin, cisplatin), and hormone therapy (e.g., tamoxifen, flutamide). The ideal antineoplastic drug would kill cancer cells selectively, with a wide therapeutic index relative to its toxicity towards non-malignant cells. It would also retain its efficacy against malignant cells even after prolonged exposure to the drug. Unfortunately, none of the current chemotherapies possess an ideal profile. Most possess very narrow therapeutic indexes, and in practically every instance cancerous cells exposed to slightly sublethal concentrations of a chemotherapeutic agent will develop resistance to such an agent, and quite often cross-resistance to several other antineoplastic agents.

Psoriasis, a common chronic skin disease characterized by the presence of dry scales and plaques, is generally thought to be the result of abnormal cell proliferation. The disease results from hyperproliferation of the epidermis and incomplete differentiation of keratinocytes. Psoriasis often involves the scalp, elbows, knees, back, buttocks, nails, eyebrows, and genital regions, and may range in severity from mild to extremely debilitating, resulting in psoriatic arthritis, pustular psoriasis, and exfoliative psoriatic dermatitis. No therapeutic cure exists for psoriasis. Milder cases are often treated with topical corticosteroids, but more severe cases may be treated with antiproliferative agents, such as the antimetabolite methotrexate, the DNA synthesis inhibitor hydroxyurea, and the microtubule disrupter colchicine.

Other diseases associated with an abnormally high level of cellular proliferation include restenosis, where vascular smooth muscle cells are involved, inflammatory disease states, where endothelial cells, inflammatory cells and glomerular cells are involved, myocardial infarction, where heart muscle cells are involved, glomerular nephritis, where kidney cells are

involved, transplant rejection, where endothelial cells are involved, infectious diseases such as HIV infection and malaria, where certain immune cells and/or other infected cells are involved, and the like. Infectious and parasitic agents per se (e.g. bacteria, trypanosomes, fungi, etc) are also subject to selective proliferative control using the subject compositions and compounds.

Accordingly, it is one object of the present invention to provide compounds which directly or indirectly upregulate LDL receptor synthesis at the level of gene expression and are useful in the treatment of hypercholesterolemia or hyperlipoproteinemia.

A further object of the present invention is to provide therapeutic compositions for treating said conditions.

A further object of the invention is to provide therapeutic compositions for treating pancreatitis.

Still further objects are to provide methods for upregulating LDL receptor synthesis, for lowering serum LDL cholesterol levels, and for preventing and treating atherosclerosis.

A further object of the present invention is to provide compounds which directly or indirectly are toxic to actively dividing cells and are useful in the treatment of cancer, viral and bacterial infections, vascular restenosis, inflammatory diseases, autoimmune diseases, and psoriasis.

A further object of the present invention is to provide therapeutic compositions for treating said conditions.

Still further objects are to provide methods for killing actively proliferating cells, such as cancerous, bacterial, or epithelial cells, and treating all types of cancers, infections, inflammatory, and generally proliferative conditions. A further object is to provide methods for treating other medical conditions characterized by the presence of rapidly proliferating cells, such as psoriasis and other skin disorders.

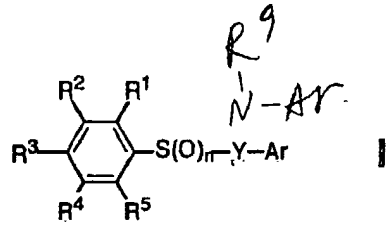
Other objects, features and advantages will become apparent to those skilled in the art from the following description and claims.

SUMMARY OF THE INVENTION

The invention provides methods and compositions relating to novel substituted benzene derivatives and analogs and their use as pharmacologically active agents. The compositions

find particular use as pharmacological agents in the treatment of disease states, particularly hypercholesterolemia, atherosclerosis, cancer, bacterial infections, and psoriasis, or as lead compounds for the development of such agents. The invention provides novel methods for treating pathology such as hypercholesterolemia, atherosclerosis, pancreatitis, and hyperlipoproteinemia, including administering to a patient an effective formulation of one or more of the subject compositions.

In one embodiment, the invention provides compounds of general Formula I:



or a pharmaceutically acceptable salt thereof, wherein:

the subscript n is 1 or 2;

R^1, R^2, R^4, and R^5 are independently selected from hydrogen, lower alkyl, halogen, OCF_3, CF_3, NO_2, CO_2H, CN, SO_2-$N(R^6)(R^7)$, SO_2-R^8, CO_2-R^8, and CO-R^8;

R^3 is a leaving group, such as halogen, NO_2, OCF_3, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, $N(R^6)$-SO_2-CF_3, $N(R^6)$-SO_2-R^8, $N(R^6)$-SO_2-Ar, $N(R^6)$-CO-R^8, $N(R^6)$-CO-Ar, $N[CO\text{-}R^8]_2$, $N(R^8)_3^+$, $N(R^8)_2(Ar)^+$, O-SO_2-Ar, O-SO_2-R^8, O-SO_2-CF_3, O-CO-(R^8), O-CO-Ar, O-Ar, O-R^8, and O-CO-CF_3;

Y is a single bond, -O-, -$N(R^9)$-, -$N(R^9)$-CH_2-, or -$CH(R^9)$-;

and Ar is an optionally substituted aryl or heteroaryl group;

wherein R^6 and R^7 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl; R^8 is selected from lower alkyl or lower heteroalkyl; and R^9 is selected from:

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

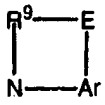
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein, if Y is -N(R^9)-, then R^9 and Ar may be connected by a linking group E to give a substituent of the Formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^9, E, Ar and the nitrogen atom contains no more than 8 atoms, or preferably R^9 and Ar may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom;

with the following provisos:

• At least one of the R^1, R^2, R^4, and R^5 groups is other than hydrogen or lower alkyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = F$, then Y is a single bond or -CH(R^9)-;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Cl$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl or unsubstituted *p*-biphenyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Br$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl;

• When R^3 = halogen, n = 2, Y = -NH- or -N(R^9)-, and at least one of R^1, R^2, R^4 and R^5 is also halogen, then at least one of R^1, R^2, R^4 and R^5 must be other than hydrogen;

• When R^1 = H, n = 2, and Y = -NH-, then at least one of R^2, R^3, R^4 and R^5 must be a substituent other than chloro;

• When $R^1 = R^5$ = H, n = 2, and Y = -N(R^9)-, then at least one of R^2, R^3, and R^4 must be a substituent other than chloro;

• When $R^1 = R^5$ = halogen, $R^2 = R^4$ = H, n = 2, and Y = -N(R^9)-, then R^3 is a substituent other than chloro or bromo;

• When $R^1 = R^2$ = halogen, $R^4 = R^5$ = H, n = 2, and Y = -N(R^9)-, then R^3 is a substituent other than chloro or bromo;

• When $R^1 = R^4$ = halogen, $R^2 = R^5$ = H, and n = 2, then R^3 is a substituent other than chloro or bromo;

• When $R^1 = R^5$ = halogen, $R^2 = R^4$ = H, and Y = -O-, then Ar is a ring system other than quinolinyl;

• When R^1 = F, $R^3 = R^4$ = Cl, and Y = -NH-, then Ar is a ring system other than 1,3,4-thiadiazolyl;

• When $R^1 = R^3$ = F, R^4 = Cl, and Y = -NH- or -O-, then Ar is a ring other than unsubstituted phenyl;

• When $R^1 = R^3 = R^5$ = Br, and Y = -NH-, then Ar is a ring other than phenyl substituted by lower-alkyl;

• When $R^1 = R^3 = R^5$ = Cl, Y = -NH-, and R^9 = H or methyl, then Ar is a phenyl ring substituted by 1-4 groups chosen independently from halogen, OH, OR', NH_2, NHR', and NR'R", wherein R' and R" are as defined below;

• When $R^2 = R^3 = R^4 = Cl$, Y = -NH-, and R^9 = propargyl, then Ar is an unsubstituted ring or a ring substituted by a group other than trifluoromethyl or nitro;

•When $R^1 = R^3 = Cl$, and Y = -N(R^9)-, then R^2 and R^4 must both be other than chloro;

• When $R^2 = CF_3$, $R^3 = Cl$, and Y = -N(R^9)-, then Ar cannot be either a phenyl ring substituted by trifluoromethyl, nitro, chloro, or lower-alkyl groups, or a 2-benzothiazolyl ring;

• When $R^2 = CO_2H$ or NO_2, $R^3 = Cl$, and Y = -N(R^9)-, then Ar is an unsubstituted phenyl or phenyl substituted by a substituent other than CO_2H or CO_2R';

• When $R^1 = NO_2$, $R^3 = Cl$, and Y = -NH-, then Ar is a ring system other than phenyl substituted by either Br or NO_2.

Substituents for the alkyl, alkoxy, alkenyl, heteroalkyl, heteroalkenyl, alkynyl, cycloalkyl, heterocycloalkyl, cycloalkenyl, and cycloalkadienyl radicals are selected independently from -H, -OH, -O-(C1-C10)alkyl, =O, $-NH_2$, -NH-(C1-C10)alkyl, -N[(C1-C10)alkyl]$_2$, -SH, -S-(C1-C10)alkyl, -halo, -Si[(C1-C10)alkyl]$_3$, in a number ranging from zero to (2N+1), where N is the total number of carbon atoms in such radical.

Substituents for the aryl and heteroaryl groups are selected independently from -halo, -OH, -O-R', -O-C(O)-R', $-NH_2$, -NHR', -NR'R", -SH, -SR', -R', -CN, $-NO_2$, $-CO_2H$, $-CO_2$-R', $-CONH_2$, -CONH-R', -CONR'R", -O-C(O)-NH-R', -O-C(O)-NR'R", -NH-C(O)-R', -NR"-C(O)-R', -NH-C(O)-OR', -NR"-C(O)-R', -NH-C(NH_2)=NH, -NR'-C(NH_2)=NH, -NH-C(NH_2)=NR', -S(O)-R', $-S(O)_2$-R', $-S(O)_2$-NH-R', $-S(O)_2$-NR'R", $-N_3$, $-CH(Ph)_2$, substituted or unsubstituted aryloxy, substituted or unsubstituted arylamino, substituted or unsubstituted heteroarylamino, substituted or unsubstituted heteroaryloxy, substituted or unsubstituted aryl-(C1-C4)alkoxy, substituted or unsubstituted heteroaryl-(C1-C4)alkoxy, perfluoro(C1-C4)alkoxy, and perfluoro(C1-C4)alkyl, in a number ranging from zero to the total number of open valences on the aromatic ring system; and where R' and R" are independently selected from substituted or unsubstituted (C1-C8)alkyl, substituted or unsubstituted (C1-C10)heteroalkyl, substituted or unsubstituted (C2-C6)alkenyl, substituted or unsubstituted (C2-C6)heteroalkenyl, substituted or unsubstituted (C2-C6)alkynyl, substituted or unsubstituted (C3-C8)cycloalkyl, substituted or unsubstituted (C3-C8)heterocycloalkyl,

substituted or unsubstituted (C5-C6)cycloalkenyl,

substituted or unsubstituted (C5-C6)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C2-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

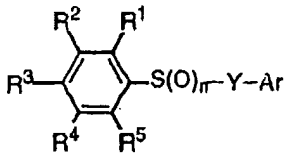
substituted or unsubstituted heteroaryl-(C2-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C1-C4)heteroalkyl.

Two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the Formula -T-C(O)-$(CH_2)_n$-U-, wherein T and U are independently selected from N, O, and C, and n = 0-2. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the Formula -A-$(CH_2)_p$-B-, wherein A and B are independently selected from C, O, N, S, SO, SO_2, and SO_2NR', and p = 1-3. One of the single bonds of the new ring so formed may optionally be replaced with a double bond. Alternatively, two of the substituents on adjacent atoms of the aryl or heteroaryl ring may optionally be replaced with a substituent of the Formula -$(CH_2)_q$-X-$(CH_2)_r$-, where q and r are independently selected from 1-3, and X is selected from O, N, S, SO, SO_2 and SO_2NR'. The substituent R' in SO_2NR' is selected from hydrogen or (C1-C6)alkyl.

In another embodiment, the invention provides for the pharmaceutical use of compounds of the general Formula I and for pharmaceutically acccptable compositions of compounds of Formula I:



or a pharmaceutically acceptable salt thereof, wherein:

the subscript n is 1 or 2; R^1, R^2, R^4, and R^5 are independently selected from hydrogen, lower alkyl, halogen, OCF_3, CF_3, NO_2, CO_2H, CN, SO_2-$N(R^6)(R^7)$, SO_2-R^8, CO_2-R^8, and CO-R^8; R^3 is a leaving group, such as halogen, NO_2, OCF_3, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, $N(R^6)$-SO_2-CF_3, $N(R^6)$-SO_2-R^8, $N(R^6)$-SO_2-Ar, $N(R^6)$-CO-R^8, $N(R^6)$-CO-Ar, $N[CO\text{-}R^8]_2$, $N(R^8)_3^+$, $N(R^8)_2(Ar)^+$, O-SO_2-Ar, O-SO_2-R^8, O-SO_2-CF_3, O-CO-(R^8), O-CO-Ar, O-Ar, O-R^8, and O-CO-CF_3; Y is a single bond, -O-, -$N(R^9)$-, -$N(R^9)$-CH_2-, or -$CH(R^9)$-; and Ar is an optionally substituted aryl or heteroaryl group; wherein R^6 and R^7 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl; R^8 is selected from lower alkyl or lower heteroalkyl; and R^9 is selected from hydrogen, substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

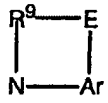
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein, if Y is -N(R^9)-, then R^9 and Ar may be connected by a linking group E to give a substituent of the Formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^9, E, Ar and the nitrogen atom contains no more than 8 atoms, or preferably R^9 and Ar may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom;

with the following provisos:

- At least one of the R^1, R^2, R^4, and R^5 groups is other than hydrogen or lower alkyl;
- When $R^1 = R^2 = R^3 = R^4 = R^5 = F$, then Y is a single bond or -CH(R^9)-;
- When $R^1 = R^2 = R^3 = R^4 = R^5 = Cl$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl or unsubstituted *p*-biphenyl;
- When $R^1 = R^2 = R^3 = R^4 = R^5 = Br$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl;
- When R^3 = halogen, n = 2, Y = -NH- or -N(R^9)-, and at least one of R^1, R^2, R^4 and R^5 is also halogen, then at least one of R^1, R^2, R^4 and R^5 must be other than hydrogen;
- When R^1 = H, n = 2, and Y = -NH-, then at least one of R^2, R^3, R^4 and R^5 must be other than chloro;

• When $R^1 = R^5 = H$, n = 2, and Y = -N(R^9)-, then at least one of R^2, R^3, and R^4 must be a substituent other than chloro;

• When $R^1 = R^3 = R^5 = Cl$, Y = -NH-, and R^9 = H or methyl, then Ar is a phenyl ring substituted by 1-4 groups chosen independently from halogen, OH, OR', NH_2, NHR', and NR'R", wherein R' and R" are as defined above;

•When $R^1 = R^3 = Cl$ and Y = -N(R^9)-, then R^2 and R^4 must both be other than chloro; and

• When $R^2 = CF_3$, $R^3 = Cl$, and Y = -N(R^9)-, then Ar cannot be either a phenyl ring substituted by trifluoromethyl, nitro, chloro, or lower-alkyl groups, or a 2-benzothiazolyl ring.

In yet another embodiment, the present invention provides novel methods for the use of pharmaceutical compositions containing compounds of the foregoing description of the general Formula I. The invention provides novel methods for treating pathology such as cancer, bacterial infections, psoriasis, hypercholesterolemia, atherosclerosis, pancreatitis, and hyperlipoproteinemia, including administering to a patient an effective formulation of one or more of the subject compositions.

DETAILED DESCRIPTION OF THE INVENTION

The term "alkyl" by itself or as part of another substituent means, unless otherwise stated, a straight or branched chain hydrocarbon radical, including di- and multi-radicals, having the number of carbon atoms designated (i.e. C1-C10 means one to ten carbons) and includes straight or branched chain groups such as methyl, ethyl, n-propyl, isopropyl, n-butyl, t-butyl, isobutyl, sec-butyl, homologs and isomers of n-pentyl, n-hexyl, 2-methylpentyl, 1,5-dimethylhexyl, 1-methyl-4-isopropylhexyl and the like. The term "alkylene" by itself or as part of another substituent means a divalent radical derived from an alkane, as exemplified by -$CH_2CH_2CH_2CH_2$-. A "lower alkyl" is a shorter chain alkyl, generally having six or fewer carbon atoms.

The term "heteroalkyl" by itself or in combination with another term means, unless otherwise stated, a stable straight or branched chain radical consisting of the stated number of carbon atoms and one or two heteroatoms selected from the group consisting of O, N, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quaternized. The heteroatom(s) may be placed at any position

of the heteroalkyl group, including between the rest of the heteroalkyl group and the fragment to which it is attached, as well as attached to the most distal carbon atom in the heteroalkyl group. Examples include -O-CH_2-CH_2-CH_3, -CH_2-CH_2-O-CH_3, -CH_2-CH_2-CH_2-OH, -CH_2-CH_2-NH-CH_3, -CH_2-CH_2-N(CH_3)-CH_3, -CH_2-S-CH_2-CH_3, -CH_2-CH_2-S(O)-CH_3, -O-CH_2-CH_2-CH_2-NH-CH_3, and -CH_2-CH_2-S(O)$_2$-CH_3. Up to two heteroatoms may be consecutive, such as, for example, -CH_2-NH-OCH_3. The term "heteroalkylene" by itself or as part of another substituent means a divalent radical derived from heteroalkyl, as exemplified by -CH_2-CH_2-S-CH_2-CH_2- and -CH_2-S-CH_2-CH_2-NH-.

The terms "cycloalkyl" and "heterocycloalkyl", by themselves or in combination with other terms represent, unless otherwise stated, cyclic versions of "alkyl" and "heteroalkyl", respectively. Examples of cycloalkyl include cyclopentyl, cyclohexyl, cycloheptyl, and the like. Examples of heterocycloalkyl include 1-piperidinyl, 2-piperidinyl, 3-piperidinyl, 4-morpholinyl, 3-morpholinyl, tetrahydrofuran-2-yl, tetrahydrofuran-3-yl, tetrahydrothien-2-yl, tetrahydrothien-3-yl, 1-piperazinyl, 2-piperazinyl, and the like.

The term "alkenyl" employed alone or in combination with other terms means, unless otherwise stated, a stable straight chain or branched monounsaturated or diunsaturated hydrocarbon group having the stated number of carbon atoms. Examples include vinyl, propenyl (allyl), crotyl, isopentenyl, butadienyl, 1,3-pentadienyl, 1,4-pentadienyl, and the higher homologs and isomers. A divalent radical derived from an alkene is exemplified by -CH=CH-CH_2-.

The term "heteroalkenyl" by itself or in combination with another term means, unless otherwise stated, a stable straight or branched chain monounsaturated or diunsaturated hydrocarbon radical consisting of the stated number of carbon atoms and one or two heteroatoms selected from the group consisting of O, N, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized and the nitrogen heteroatom may optionally be quarternized. Up to two heteroatoms may be placed consecutively. Examples include -CH=CH-O-CH_3, -CH=CH-CH_2-OH, -CH_2-CH=N-OCH_3, -CH=CH-N(CH_3)-CH_3, and -CH_2-CH=CH-CH_2-SH.

The term "alkynyl" employed alone or in combination with other terms means, unless otherwise stated, a stable straight chain or branched hydrocarbon group having the stated

A "leaving group" is defined as any substituent on an aromatic ring that can be displaced by a heteroatom nucleophile (particularly a sulfhydryl group) under a variety of conditions of solvent, pH, ionic strength and temperature. The chemical reaction in which an aromatic leaving group is replaced by a nucleophile is known as an "aromatic substitution" or "S_NAr" reaction. Reactions of the S_NAr type are often called addition-elimination reactions and proceed in solution through a σ-complex called the Meisenheimer complex. Depending on the nature of the leaving group the Meisenheimer complex can be an intermediate or a transition state. The concept of the leaving group in an S_NAr reaction is elaborated further in *Advanced Organic Chemistry*, by Jerry March, 2nd Edition, McGraw-Hill, New York: 1997, pages 594-595, and references in footnote 2, Chapter 13 of the same textbook. Examples of leaving groups include: fluoro, chloro, bromo, iodo, nitro, trifluoromethoxy, Ph-S(O)-, azido, CF_3SO_2NH-, $PhSO_2NH$-, trimethylammonium, $PhOSO_2$-, and trifluoroacetate. In addition to the leaving groups listed in the specifications of the present invention, it is also possible to identify additional leaving groups, also included in the present invention, by performing mathematical calculations to evaluate the ability of compounds of Formula I to undergo S_NAr reactions with a thiolate nucleophile. This is achieved by first performing *ab initio* quantum mechanical calculations and geometry optimization in the reaction intermediates and complexes. This is followed by calculation of their energy and thermodynamic properties. The *ab initio* calculations can be carried out at the HF/6-31+G** level of theory using programs such as GAUSSIAN 94 from Gausssian Inc., Pittburg PA. The solvation free enegy is then calculated from the *ab initio* results using a program that models the solvent effect. This is achieved by using commercially available programs such as PS-GVB. The overall free energy for the S_NAr reaction is obtained by adding the gas phase and solution free energy profiles. Using this approach, one can calculate the free energy barrier for specific componds of Formula I as they undergo S_NAr reaction with thiolate ions in aqueous solution. Zheng and *Ornstein (J. Am. Chem. Soc.*, **1997**, *119*, 648-655) have developed and applied this method for the evaluation of the S_NAr reaction between 1-chloro-2,4-dinitrobenzene and a thiolate ion, and found that, at the HF/6-31+G** level of theory, the theoretical and experimental energy values are in good agreement.

number of carbon atoms, and containing one or two carbon-carbon triple bonds, such as ethynyl, 1- and 3-propynyl, 4-but-1-ynyl, and the higher homologs and isomers.

The term "alkoxy" employed alone or in combination with other terms means, unless otherwise stated, an alkyl group, as defined above, connected to the rest of the molecule via an oxygen atom, such as, for example, methoxy, ethoxy, 1-propoxy, 2-propoxy and the higher homologs and isomers.

The terms "halo" or "halogen" by themselves or as part of another substituent mean, unless otherwise stated, a fluorine, chlorine, bromine, or iodine atom.

The term "aryl" employed alone or in combination with other terms means, unless otherwise stated, a phenyl, 1-naphthyl, or 2-naphthyl group. The maximal number of substituents allowed on each one of these ring systems is five, seven, and seven, respectively. Substituents are selected from the group of acceptable substituents listed above.

The term "heteroaryl" by itself or as part of another substituent means, unless otherwise stated, an unsubstituted or substituted, stable, mono- or bicyclic heterocyclic aromatic ring system which consists of from four to ten carbon atoms and from one to four heteroatoms selected from the group consisting of N, O, and S, and wherein the nitrogen and sulfur atoms may optionally be oxidized, and the nitrogen atom(s) may optionally be quaternized. The heterocyclic system may be attached, unless otherwise stated, at any heteroatom or carbon atom which affords a chemically stable structure. The heterocyclic system may be substituted or unsubstituted with one to four substituents independently selected from the list of acceptable aromatic substituents listed above. Examples of such heterocycles include 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 3-pyrazolyl, 2-imidazolyl, 4-imidazolyl, pyrazinyl, 2-oxazolyl, 4-oxazolyl, 5-oxazolyl, 3-isoxazolyl, 4-isoxazolyl, 5-isoxazolyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrimidyl, 4-pyrimidyl, 5-benzothiazolyl, purinyl, 2-benzimidazolyl, 5-indolyl, 1-isoquinolyl, 5-isoquinolyl, 2-quinoxalinyl, 5-quinoxalinyl, 3-quinolyl, and 6-quinolyl.

The term "lower" used alone or in combination with another term indicates that a radical or substituent group contains a total number of heavy atoms (carbon, oxygen, nitrogen, etc) between one and ten.

Pharmaceutically acceptable salts of the compounds of Formula I include salts of these compounds with relatively nontoxic acids or bases, depending on the particular substituents found on specific compounds of Formula I. When compounds of Formula I contain relatively acidic functionalities, base addition salts can be obtained by contacting the neutral form of compound I with a sufficient amount of the desired base, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable base addition salts include sodium, potassium, calcium, ammonium, organic amino, or magnesium salt, or a similar salt. When compounds of Formula I contain relatively basic functionalities, acid addition salts can be obtained by contacting the neutral form of compound I with a sufficient amount of the desired acid, either neat or in a suitable inert solvent. Examples of pharmaceutically acceptable acid addition salts include those derived from inorganic acids like hydrochloric, hydrobromic, nitric, carbonic, monohydrogencarbonic, phosphoric, monohydrogenphosphoric, dihydrogenphosphoric, sulfuric, monohydrogensulfuric, hydriodic, or phosphorous acids and the like, as well as the salts derived from relatively nontoxic organic acids like acetic, propionic, isobutyric, oxalic, maleic, malonic, benzoic, succinic, suberic, fumaric, mandelic, phthalic, benzenesulfonic, p-tolylsulfonic, citric, tartaric, methanesulfonic, and the like. Also included are salts of amino acids such as arginate and the like, and salts of organic acids like gluconic or galactunoric acids and the like (see, for example, Berge, S.M., et al, "Pharmaceutical Salts", *Journal of Pharmaceutical Science*, 1977, *66*, 1-19). Certain specific compounds of Formula I contain both basic and acidic functionalities that allow the compounds to be converted into either base or acid addition salts.

The neutral forms of the compounds may be regenerated by contacting the salt with a base or acid and isolating the parent compound in the conventional manner. The parent form of the compound differs from the various salt forms in certain physical properties, such as solubility in polar solvents, but otherwise the salts are equivalent to the parent form of the compound for the purposes of the present invention.

Certain compounds of the present invention can exist in unsolvated forms as well as solvated forms, including hydrated forms. In general, the solvated forms are equivalent to unsolvated forms and are intended to be encompassed within the scope of the present invention.

Certain compounds of the present invention possess asymmetric carbon atoms (optical centers); the racemates, diastereomers, and individual isomers are all intended to be encompassed within the scope of the present invention.

The compounds of the present invention may also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the compounds may be radiolabeled with radioactive isotopes, such as for example tritium (^{3}H) or carbon-14 (^{14}C). All isotopic variations of the compounds of the present invention, whether radioactive or not, are intended to be encompassed within the scope of the present invention.

Illustrative examples of compounds and pharmaceutical compositions of the subject pharmaceutical methods include:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-[(3-Chloro-4-methoxyphenyl)aminosulfonyl]-2,3,4-trifluorobenzene;

2,3,4-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

4-Fluoro-1-[(4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-(Diacetylamino)-2,3-difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-5-nitrobenzene;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Chloro-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulphenyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3,4-dimethoxyphenyl)methylsulfonyl]benzonitrile;

2,3,4-Trifluoro-5-[(4-dimethylaminophenyl)sulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)sulfenyl]benzoic acid, ethyl ester;

1-Chloro-4-[(4-methoxyphenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)sulfonyl]-2-nitrobenzene;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene; and

4,5-Difluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

There are several preferred embodiments of the present invention. In one such preferred embodiment, compounds of general Formula **I**, or a pharmaceutically acceptable salt thereof, are preferred in which R^1, R^2, R^4, and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, SO_2-(lower-alkyl), NO_2, CN, and SO_2-$N(R^6)(R^7)$; R^3 is halogen or OCF_3; n = 2; Y is a single bond, -$N(R^9)$-, or -$CH(R^9)$-; Ar is an optionally substituted aryl or heteroaryl group; and R^6, R^7 and R^9 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl.

Also preferred are compounds of Formula I in which there is no linking group E between R^9 and Ar.

Most preferred are compounds of Formula **I** in which R^1, R^2, R^4, and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, and CN; R^3 is halogen or OCF_3; Y is -NH-; n = 2; Ar is an optionally substituted aryl group; R^6 and R^7 are independently selected from lower-alkyl; and R^9 is hydrogen.

Preferred compounds and compositions of this embodiment of the invention have specific pharmacological properties. Examples of the most preferred compounds and compositions of this embodiment of the invention include:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-fluorobenzonitrile;

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2- [(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene; or

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene.

1-Chloro-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

4-Trifluoromethoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

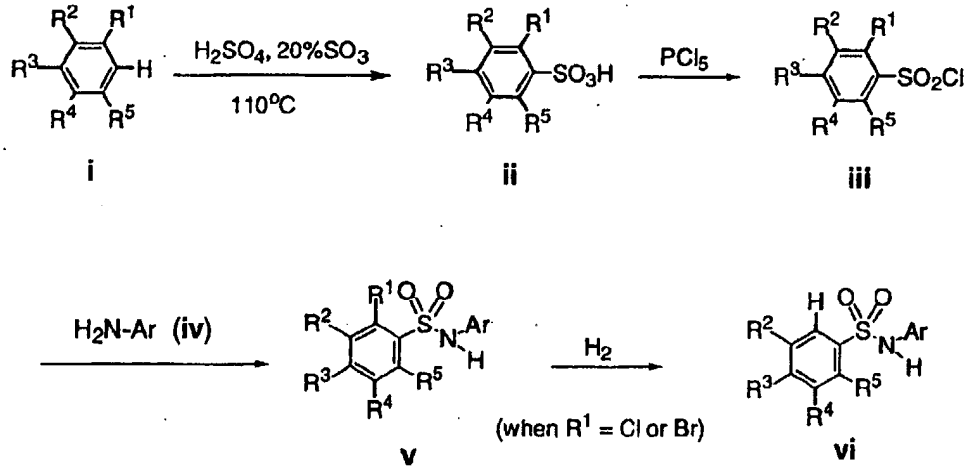
2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

SYNTHESIS

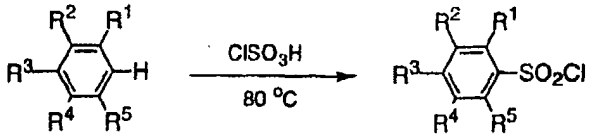
The invention provides methods of making the subject compounds and compositions. In one general embodiment, the methods involve combining an appropriate sulfonyl chloride (iii) with an appropriate aniline (iv), as outlined in Scheme 1, to yield a sulfonamide (v). The necessary sulfonyl chlorides (iii) can be prepared by sulfonation of the appropriately substituted aromatic compounds (i) with fuming sulfuric acid, followed by treatment with a chlorinating agent, such as PCl_5, $POCl_3$ and the like, to afford the corresponding sulfonyl chlorides (iii), (Scheme 1). When the sulfonamides contain certain groups, such as chloro or bromo, these groups can be catalytically reduced to produce yet other analogous sulfonamides (vi).

Scheme 1



An alternative way of preparing the desired sulfonyl chlorides (iii) is by heating the starting aromatic compounds (i) with chlorosulfonic acid as shown in Scheme 2.

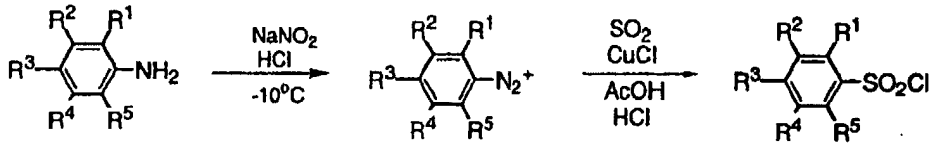
Scheme 2



i iii

Alternatively, the desired sulfonyl chlorides (iii) are prepared from their corresponding anilines (vii) by dissolving the aniline in an acidic aqueous solution, such as HCl and the like, followed by addition of an aqueous solution of sodium nitrite at a temperature below ambient temperature, typically between -20 and +5 °C. The resulting mixture, containing the desired diazonium salt, is then added to a saturated solution of sulfur dioxide in glacial acetic acid containing cuprous chloride, at a temperature between -10 and +10 °C, to yield the corresponding sulfonyl chloride (iii) (see Scheme 3).

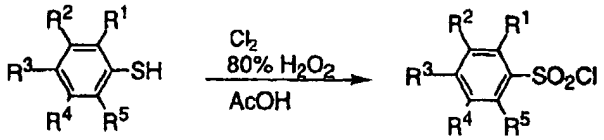
Scheme 3



vii viii iii

The desired sulfonyl chlorides (iii) can also be prepared by oxidation of the respective thiophenols (ix) with chlorine and hydrogen peroxide in acetic acid as shown in Scheme 4.

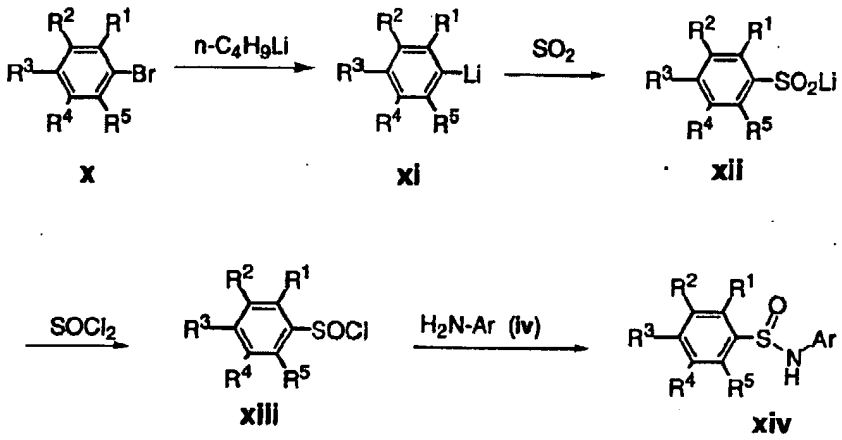
Scheme 4



ix iii

The sulphinamides described in this patent can be synthesized by reaction of the desired sulphinyl chlorides (xiii) with the appropriate amine (iv), as shown in Scheme 5. The necessary sulphinyl chlorides (xiii) are prepared by metal-halogen exchange reaction on the appropriate aryl bromides (x), chlorides or iodides, with an alkyllithium reagent such as butyl-lithium, or with magnesium metal, followed by treatment of the resulting aryl organometallic compounds (xi) with sulfur dioxide affords the lithium sulfinates (xii) that can be further reacted with thionyl chloride to afford the desired sulphinyl chlorides (xiii).

Scheme 5

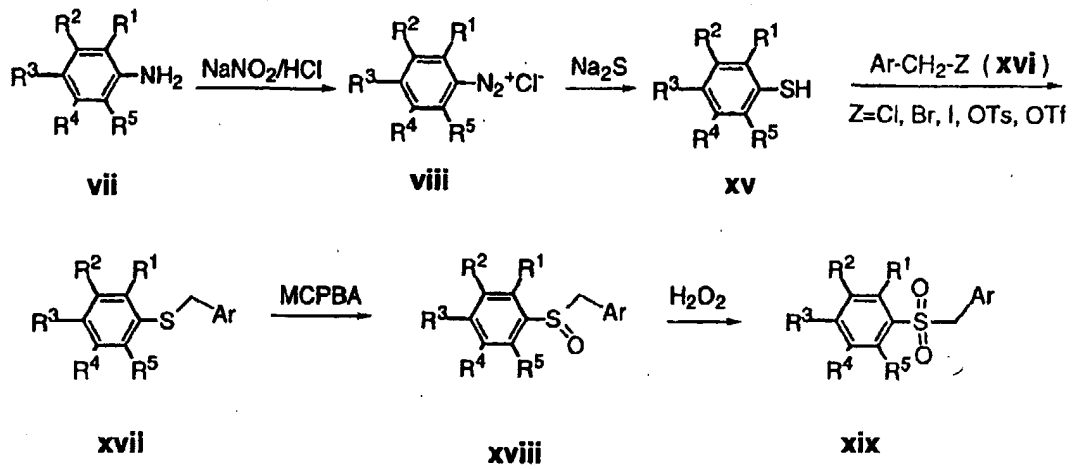


x xi xii xiii xiv

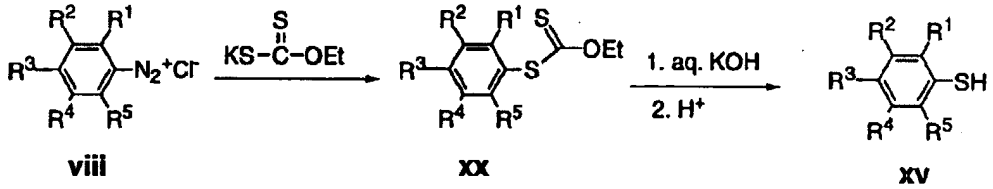
The sulfoxides (xviii) and sulfones (xix) described in this patent can be prepared by reaction of the desired substituted thiophenols (xv) with the derivatized benzylic halides (xvi) to yield the corresponding sulfides (xvii), which can be oxidized to the corresponding sulfoxides (xviii) or sulfones according to Scheme 6. The necessary thiophenols (xv) can be prepared from the starting substituted anilines (vii) by diazotization, followed by treatment with sodium sulfide (Scheme 6).

Alternatively, the thiophenols (xv) can be prepared by treatment of the diazonium salts (viii) with potassium ethyl xanthate, followed by saponification of the resulting xanthates (xx), as shown in Scheme 7. Other alternate methods for the synthesis of the desired substituted thiophenols (xv) are described in the chemical literature and should be well known to individuals versed in the art of organic synthesis.

Scheme 6



Scheme 7



In cases where the desired compounds of Formula I contain one or more bromine, chlorine, or iodide atoms, these can be hydrogenated in the presence of a catalyst, such as palladium on carbon, to give the corresponding dehalogenated compounds. This process is outlined in Scheme 1. The compounds used as initial starting materials in this invention may be purchased from commercial sources or alternatively are readily synthesized by standard procedures which are well know to those of ordinary skill in the art.

Some of the compounds of Formula I may exist as stereoisomers, and the invention includes all active stereoisomeric forms of these compounds. In the case of optically active isomers, such compounds may be obtained from corresponding optically active precursors using the procedures described above or by resolving racemic mixtures. The resolution may be

carried out using various techniques such as chromatography, repeated recrystallization of derived asymmetric salts, or derivatization, which techniques are well known to those of ordinary skill in the art.

The compounds of the invention may be labeled in a variety of ways. For example, the compounds may contain radioactive isotopes such as, for example, ^{3}H (tritium) and ^{14}C (carbon-14). Similarly, the compounds may be advantageously joined, covalently or noncovalently, directly or through a linker molecule, to a wide variety of other compounds, which may provide pro-drugs or function as carriers, labels, adjuvents, coactivators, stabilizers, etc. Such labeled and joined compounds are contemplated within the present invention.

Analysis of Compounds

The subject compounds and compositions were demonstrated to have pharmacological activity in *in vitro* and *in vivo* assays, e.g., they are capable of specifically modulating a cellular physiology to reduce an associated pathology or provide or enhance a prophylaxis.

Certain preferred compounds and compositions are capable of specifically regulating LDL receptor gene expression. Compounds may be evaluated *in vitro* for their ability to increase LDL receptor expression using western-blot analysis, for example, as described in Tam et al. (*J. Biol. Chem.* **1991**, *266*, 16764). Established animal models to evaluate hypocholesterolemic effects of compounds are known in the art. For example, compounds disclosed herein are shown to lower cholesterol levels in hamsters fed a high-cholesterol diet, using a protocol similar to that described in Spady et al. (*J. Clin. Invest.* **1988**, *81*, 300), Evans et al. (*J. Lipid Res.* **1994**, *35*, 1634), and Lin et al (*J. Med. Chem.* **1995**, *38*, 277).

Certain preferred compounds and compositions display specific toxicity to various types of cells. Certain compounds and compositions of the present invention exert their cytotoxic effects by interacting with cellular tubulin. For certain preferred compounds and compositions of the present invention, that interaction is covalent and irreversible. Compounds and compositions may be evaluated *in vitro* for their ability to inhibit cell growth, for example, as described in Ahmed et al. (*J. Immunol. Methods* **1994**, *170*, 211). Established animal models to evaluate antiproliferative effects of compounds are known in the art. For example,

compounds can be evaluated for their ability to inhibit the growth of human tumors grafted into immunodeficient mice using methodology similar to that described by Rygaard and Povlsen (*Acta Pathol. Microbiol. Scand.* **1969**, *77*, 758) and Giovanella and Fogh (*Adv. Cancer Res.* **1985**, *44*, 69).

Formulation and Administration of Compounds and Pharmaceutical Compositions

The invention provides methods of using the subject compounds and compositions to treat disease or provide medicinal prophylaxis, to upregulate LDL receptor gene expression in a cell, to reduce blood cholesterol concentration in a host, to slow down and/or reduce the growth of tumors, etc. These methods generally involve contacting the cell with or administering to the host an effective amount of the subject compounds or pharmaceutically acceptable compositions.

The compositions and compounds of the invention and the pharmaceutically acceptable salts thereof can be administered in any effective way such as via oral, parenteral or topical routes. Generally, the compounds are administered in dosages ranging from about 2 mg up to about 2,000 mg per day, although variations will necessarily occur depending on the disease target, the patient, and the route of administration. Preferred dosages are administered orally in the range of about 0.05 mg/kg to about 20 mg/kg, more preferably in the range of about 0.05 mg/kg to about 2 mg/kg, most preferably in the range of about 0.05 mg/kg to about 0.2 mg per kg of body weight per day.

In one embodiment, the invention provides the subject compounds combined with a pharmaceutically acceptable excipient such as sterile saline or other medium, water, gelatin, an oil, etc. to form pharmaceutically acceptable compositions. The compositions and/or compounds may be administered alone or in combination with any convenient carrier, diluent, etc. and such administration may be provided in single or multiple dosages. Useful carriers include solid, semi-solid or liquid media including water and non-toxic organic solvents.

In another embodiment, the invention provides the subject compounds in the form of a pro-drug, which can be metabolically converted to the subject compound by the recipient host. A wide variety of pro-drug formulations are known in the art.

The compositions may be provided in any convenient form including tablets, capsules, lozenges, troches, hard candies, powders, sprays, creams, suppositories, etc. As such the compositions, in pharmaceutically acceptable dosage units or in bulk, may be incorporated into a wide variety of containers. For example, dosage units may be included in a variety of containers including capsules, pills, etc.

The compositions may be advantageously combined and/or used in combination with other hypocholesterolemic or antiproliferative therapeutic or prophylactic agents, different from the subject compounds. In many instances, administration in conjunction with the subject compositions enhances the efficacy of such agents. Examplary antiproliferative agents include cyclophosphamide, methotrexate, adriamycin, cisplatin, daunomycin, vincristine, vinblastine, vinarelbine, paclitaxel, docetaxel, tamoxifen, flutamide, hydroxyurea, and mixtures thereof. Exemplary hypocholesterolemic and/or hypolipemic agents include: bile acid sequestrants such as quaternary amines (e.g. cholestyramine and colestipol); nicotinic acid and its derivatives; HMG-CoA reductase inhibitors such as mevastatin, pravastatin, and simvastatin; gemfibrozil and other fibric acids, such as gemfibrozil, clofibrate, fenofibrate, benzafibrate and cipofibrate; probucol; raloxifene and its derivatives; and mixtures thereof.

The compounds and compositions also find use in a variety of *in vitro* and *in vivo* assays, including diagnostic assays. For example, various allotypic LDL receptor gene expression processes may be distinguished in sensitivity assays with the subject compounds and compositions, or panels thereof. In certain assays and in *in vivo* distribution studies, it is desirable to used labeled versions of the subject compounds and compositions, e.g. radioligand displacement assays. Accordingly, the invention provides the subject compounds and compositions comprising a detectable label, which may be spectroscopic (e.g. fluorescent), radioactive, etc.

The following examples are offered by way of illustration and not by way of limitation.

EXAMPLES

^{1}H-NMR spectra were recorded on a Varian Gemini 400 MHz NMR spectrometer. Significant peaks are tabulated in the order: number of protons, multiplicity (s, singlet; d,

doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet) and coupling constant(s) in Hertz. Electron Ionization (EI) mass spectra were recorded on a Hewlett Packard 5989A mass spectrometer. Mass spectrometry results are reported as the ratio of mass over charge, followed by the relative abundance of each ion (in parentheses).

Preparation of Synthetic Intermediates

The majority of the starting materials for the synthesis of the examples of the present invention are available from commercial sources or are known compounds described in the published literature. Literature references of general utility to the following examples include:

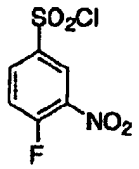
1) *Organic Syntheses, Coll. Vol. VII*; **1990**, Jeremiah P. Freeman, ed., John Wiley & Sons, 508-511.

2) Robson, P., Smith, T.A., Stephens, R., Tatlow, J., *J. Chem. Soc.*, **1963**, 3692-3703.

3) *Synthesis of Fluoroorganic Compounds*; **1985**, Knunyants, I. and Yakobson, G., eds., Springer-Verlag,190.

The synthesis of a selected group of starting materials that have not been described previously is exemplified as follows:

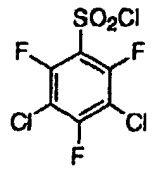
Example A



4-Fluoro-3-nitrophenylsulfonyl chloride.

2-Fluoronitrobenzene (10.0 g, 70.9 mmol) was added to chlorosulfonic acid (10.0 ml, 150 mmol) at 65 °C. After stirring at 85 °C for 18 h, the reaction mixture was cooled to room temperature and poured onto ice chips and extracted with CH_2Cl_2 (2 x 250 ml). The combined organic extracts were washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$). Concentration at room temperature and then at 100 °C under high vacuum produced 2.40 g (14%) of the title compound as a yellow oil. ^{1}H-NMR ($CDCl_3$): ∂ 8.76 (1H, dd, J = 2.4, 6.5 Hz), 8.33 (1H, ddd, J = 2.4, 3.8, 9.2 Hz), 7.61 (1H, t, J = 9.2 Hz). MS (EI): 239 (15, M^+), 204 (100).

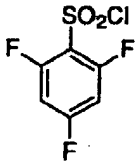
Example B



3,5-Dichloro-2,4,6-trifluorophenylsulfonyl chloride.

1,3-Dichloro-2,4,6-trifluorobenzene (5.0 g, 25 mmol) and chlorosulfonic acid (10.0 ml, 150 mmol) were mixed at ambient temperature under a nitrogen atmosphere and the reaction was heated at 80 °C for 24 h. The mixture was then allowed to cool to ambient temperature and was poured onto 12 g of crushed ice. The product was extracted with diethyl ether, dried over $MgSO_4$, and evaporated to produce 4.9 g of the title compound, which was used without further purification. MS (EI): 300 (30, M^+), 298 (28), 263 (100), 199 (80).

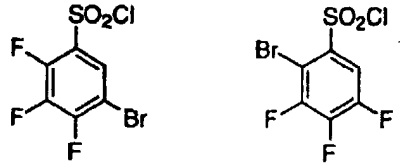
Example C



2,4,6-Trifluorophenylsulfonyl chloride.

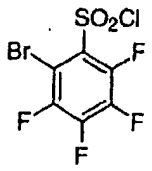
The title compound was synthesized from 1,3,5-trifluorobenzene by a method similar to that used in Example B. MS (EI): 230 (20, M^+), 195 (80), 131 (50), 81 (100).

Examples D and E



5-Bromo-2,3,4-trifluorophenylsulfonyl chloride (Example D) and 2-Bromo-3,4,5-trifluorophenylsulfonyl chloride (Example E). The title compounds were obtained as a mixture from 1-bromo-2,3,4-trifluorobenzene by a method similar to that used in Example B.

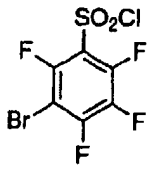
Example F



2-Bromo-3,4,5,6-tetrafluorophenylsulfonyl chloride.

1-Bromo-2,3,4,5-tetrafluorobenzene (5.0 g, 21.8 mmol) was mixed at ambient temperature with 20% fuming sulfuric acid (20 ml). The mixture was heated at 40 °C for 3 h and at 110 °C for 2 h. The reaction mixture was allowed to cool to ambient temperature and poured onto 12 g of crushed ice. The mixture was acidified dropwise with concentrated HCl (2 ml) until a solid, consisting mostly of 2-bromo-3,4,5,6-tetrafluorophenylsulfonic acid was formed. The solid was filtered, washed with 12N HCl, and dried under high vacuum to afford 5.3 g of 2-bromo-3,4,5,6-tetrafluorophenylsulfonic acid as a white hygroscopic solid that was used without further purification. To the sulfonic acid (3.0 g, 9.7 mmol) was then added phosphorous pentachloride (8.0 g, 38.4 mmol) in small portions, at ambient temperature (*Caution: exothermic reaction with significant evolution of HCl*). The reaction was allowed to stir for 20 minutes after the final addition of phosphorous pentachloride. The reaction mixture was then poured onto crushed ice and the white solid that formed was filtered and dried to afford 2.8 g of the title compound, which was used without further purification. MS (EI): 328 (30, M^+), 293 (70), 229 (30), 148 (100).

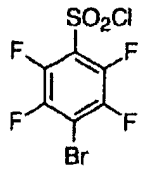
Example G



3-Bromo-2,4,5,6-tetrafluorophenylsulfonyl chloride.

The title compound was synthesized from 1-bromo-2,3,4,6-tetrafluorobenzene by a method similar to that used in Example F. MS (EI): 328 (20, M^+), 293 (70), 229 (50), 148 (100).

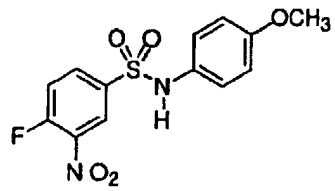
Example H



4-Bromo-2,3,5,6-tetrafluorophenylsulfonyl chloride.

The title compound was synthesized from 1-bromo-2,3,5,6-tetrafluorobenzene by a method similar to that used in Example F. MS (EI): 328 (20, M^+), 293 (70), 229 (50), 148 (100).

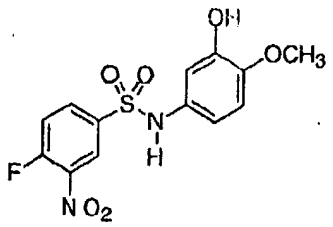
Example 1



4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene.

p-Anisidine (760 mg, 6.18 mmol) was added to a solution of 4-fluoro-3-nitrophenylsulfonyl chloride (740 mg, 3.09 mmol) in MeOH (10 ml) at ambient temperature. After stirring at room temperature for 15 min, the reaction mixture was concentrated under reduced pressure and the residue was taken up in ethyl acetate and filtered through a pad of silica gel. Concentration of the filtrate, followed by chromatography, provided 603 mg (60% yield) of the title compound. ^{1}H-NMR ($CDCl_3$): ∂ 8.42 (1H, dd, J = 2.3, 6.8 Hz), 7.88 (1H, ddd, J = 2.4, 4.0, 8.8 Hz), 7.33 (1H, dd, J = 8.8, 9.9 Hz), 6.98 (2H, m), 6.81 (2H, m), 6.45 (1H, s), 3.77 (3H, s). MS (EI): 326 (11, M^+), 122 (100). Anal. Calcd. for $C_{13}H_{11}FN_2O_5S$: C, 47.85; H, 3.40; N, 8.59; S, 9.83. Found: C, 47.68; H, 3.44; N, 8.54; S, 9.88.

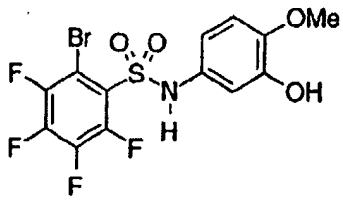
Example 2



4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene.

The title compound was prepared in a manner similar to that described in Example 1, by replacing *p*-anisidine with 3-hydroxy-4-methoxyaniline. ^{1}H-NMR ($CDCl_3$): ∂ 8.41 (1H, dd, *J* = 2.4, 6.7 Hz), 7.92 (1H, m), 7.14 (1H, ddd, *J* = 2.4, 4.0, 9.0 Hz), 7.35 (1H, dd, *J* = 9.6, 9.0 Hz), 6.72 (1H, d, *J* = 8.5 Hz), 6.62 (1H, d, *J* = 2.5 Hz), 6.58 (1H, dd, *J* = 2.5, 8.5 Hz), 6.44 (1H, s), 5.64 (1H, s), 3.85 (3H, s). Anal. Calcd. for $C_{13}H_{11}FN_2O_6S$: C, 45.62; H, 3.24; N, 8.18; S, 9.37. Found: C, 45.71; H, 3.25; N, 8.17; S, 9.29.

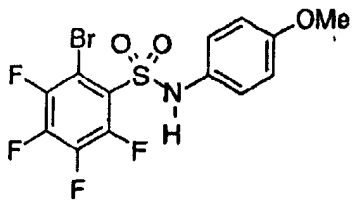
Example 3



1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing *p*-anisidine with 3-hydroxy-4-methoxyaniline and replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2-bromo-3,4,5,6-tetrafluorophenylsulfonyl chloride (Example F). ^{1}H-NMR ($CDCl_3$): ∂ 7.28 (br s, 1H), 6.69 (m, 3H), 5.72 (s, 1H), 3.82 (s, 3H). MS (EI): 431 (20), 429 (20), 138 (100). Anal. calcd. for $C_{13}H_8BrF_4NO_4S$: C, 36.30; H, 1.87; N, 3.26; S, 7.45. Found: C, 36.20; H, 1.90; N, 3.31; S, 7.39.

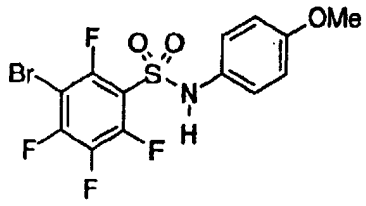
Example 4



1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2-bromo-3,4,5,6-tetrafluorophenylsulfonyl chloride (Example F). ^{1}H-NMR ($CDCl_3$): ∂ 7.23 (1H, br s), 7.07 (2H, dd, *J*=9.0 and 2.0 Hz), 6.78 (2H, dd, *J*=9.0 and 2.0 Hz), 3.75 (3H, s). MS (EI): 415/413 (10, M^+), 122 (100). Anal. Calcd. for $C_{13}H_8BrF_4NO_3S$: C, 37.70; H, 1.95; N, 3.38; S, 7.74. Found: C, 37.60; H, 1.92; N, 3.30; S, 7.71.

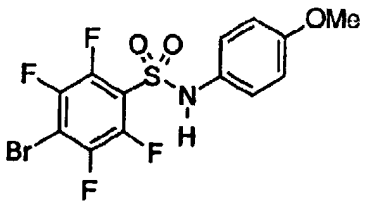
Example 5



1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 3-bromo-2,4,5,6-tetrafluorophenylsulfonyl chloride (Example G). ^{1}H-NMR ($CDCl_3$): ∂ 7.10 (2H, dd, *J* = 9.0 and 2.0 Hz), 7.07 (1H, br s), 6.82 (2H, dd, *J* = 9.0 and 2.0 Hz), 3.77 (3H, s). MS(EI): 415/413 (10, M^+), 122 (100). Anal. Calcd. for $C_{13}H_8BrF_4NO_3S$: C, 37.70; H, 1.95; N, 3.38; S, 7.74. Found: C, 37.66; H, 1.94; N, 3.33; S, 7.67.

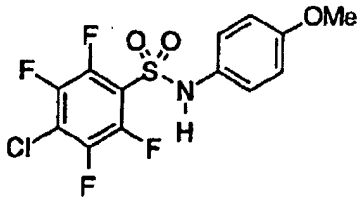
Example 6



1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 4-bromo-2,3,5,6-tetrafluorophenylsulfonyl chloride (Example H). ^{1}H-NMR ($CDCl_3$): ∂ 7.16 (1H, br s), 7.11 (2H, dd, J = 9.0 and 2.0 Hz), 6.82 (2H, dd, J = 9.0 and 2.0 Hz), 3.77 (3H, s). MS(EI): 415/413 (10, M^+), 122 (100). Anal. Calcd. for $C_{13}H_8BrF_4NO_3S$: C, 37.70; H, 1.95; N, 3.38; S, 7.74. Found: C, 37.62; H, 1.95; N, 3.34; S, 7.66.

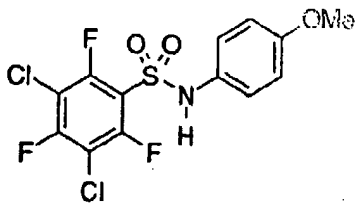
Example 7



1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 4-chloro-2,3,5,6-tetrafluorophenylsulfonyl chloride. ^{1}H-NMR ($CDCl_3$): ∂ 7.12 (2H, d, J = 9.0 Hz), 6.90 (1H, br s), 6.83 (2H, J = 9.0 Hz), 3.78 (3H, s). MS(EI): 369 (20, M^+), 122 (100).

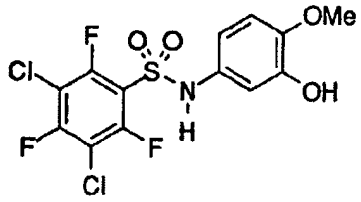
Example 8



1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 3,5-dichloro-2,4,6-trifluorophenylsulfonyl chloride (Example B). ^{1}H-NMR ($CDCl_3$): ∂ 7.09 (2H, d, J = 9.0 Hz), 6.85 (1H, br s), 6.82 (2H, d, J = 9.0 Hz), 3.77 (3H, s). MS (EI): 386 (15, M^+), 385 (20), 122 (100). Anal. Calcd. for $C_{13}H_8Cl_2F_3NO_3S$: C, 40.43; H, 2.09; N, 3.63; S, 8.30. Found: C, 40.34; H, 2.06; N, 3.70; S, 8.22.

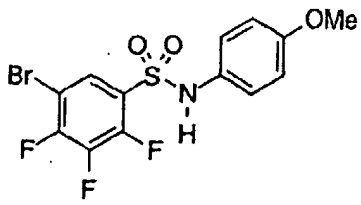
Example 9



1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing *p*-anisidine with 3-hydroxy-4-methoxyaniline and replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 3,5-dichloro-2,4,6-trifluorophenylsulfonyl chloride (Example B). ^{1}H-NMR ($CDCl_3$): ∂ 6.88 (1H, br s), 6.7-6.8 (3H, m), 5.66 (1H, s), 3.85 (3H, s). MS(EI): 402 (15, M^+), 401 (20), 138 (100). Anal. Calcd. for $C_{13}H_8Cl_2F_3NO_4S$: C, 38.83; H, 2.00; N, 3.48; S, 7.97. Found: C, 38.66; H, 1.97; N, 3.39; S, 7.86.

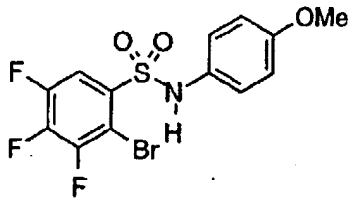
Example 10



1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene.

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene (Example 10) and 1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene (Example 11) were prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with a mixture of 5-bromo-2,3,4-trifluorophenylsulfonyl chloride (Example D) and 2-bromo-3,4,5-trifluorophenylsulfonyl chloride (Example E). The two isomeric compounds were separated by column chromatography (silica gel; ethyl acetate:hexanes, 1:4). ^{1}H-NMR ($CDCl_3$): ∂ 7.76 (1H, m), 7.04 (2 H; d, J = 9.0 Hz), 6.82 (1H, br s), 6.80 (2H, d, J = 9.0 Hz), 3.75 (3H, s). MS(EI): 397/395 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_9BrF_3NO_3S$: C, 39.41; H, 2.29; N, 3.54; S, 8.08. Found: C, 39.34; H, 2.23; N, 3.47; S, 7.99.

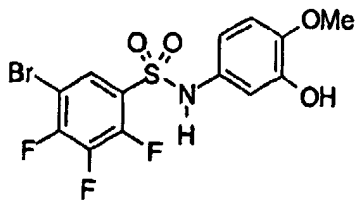
Example 11



1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene.

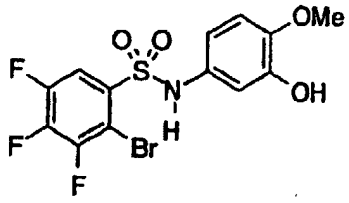
^{1}H-NMR ($CDCl_3$): ∂ 7.69 (1H, m), 7.08 (1H, br s), 7.03 (2H, dd, J = 9.0 and 2.0 Hz), 6.76 (2H, dd, J = 9.0 and 2.0 Hz), 3.75 (3H, s). MS(EI): 397/395 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_9BrF_3NO_3S$: C, 39.41; H, 2.29; N, 3.54; S, 8.08. Found: C, 39.32; H, 2.31; N, 3.44; S, 7.99.

Example 12



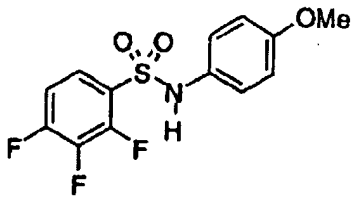
1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene. 1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene (Example 12) and 1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene (Example 13) were prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with a mixture of 5-bromo-2,3,4-trifluorophenylsulfonyl chloride (Example D) and 2-bromo-3,4,5-trifluorophenylsulfonyl chloride (Example E) and replacing *p*-anisidine with 3-hydroxy-4-methoxyaniline. The two isomeric compounds were separated by column chromatography (silica gel; ethyl acetate:hexanes, 1:4). ^{1}H-NMR ($CDCl_3$): ∂ 7.79 (1H, m), 6.72-6.62 (4H, m), 5.65 (1H, s), 3.85 (3H, s).

Example 13



1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene. ^{1}H-NMR ($CDCl_3$): ∂ 7.73 (1H, m), 6.94 (1H, br s), 6.72-6.62 (3H, m), 5.63 (1H, s), 3.83 (3H, s).

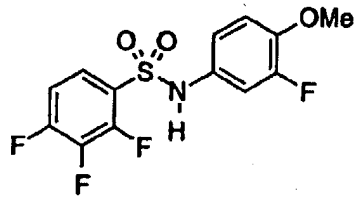
Example 14



2,3,4-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2,3,4-trifluorophenylsulfonyl chloride. ^{1}H-NMR ($CDCl_3$): ∂ 7.51 (1H, m), 7.02 (3H, m), 6.78 (2H, dd, J = 9.0 and 2.0 Hz), 6.65 (1H, br s), 3.76 (3H, s). MS(EI): 317 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_{10}F_3NO_3S$: C, 49.21; H, 3.18; N, 4.41; S, 10.10. Found: C, 49.10; H, 3.14; N, 4.32; S, 9.99.

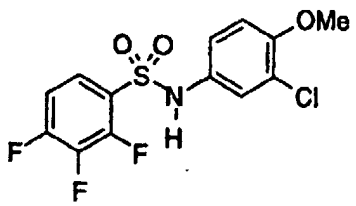
Example 15



2,3,4-Trifluoro-1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]ybenzene.

The title compound was prepared in a manner similar to that described in Example 1, by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2,3,4-trifluorophenylsulfonyl chloride and replacing *p*-anisidine with 3-fluoro-4-methoxyaniline. ^{1}H-NMR ($CDCl_3$): ∂ 7.52 (1H, m), 7.00 (1H, m), 6.93 (1H, m), 6.80 (2H, m), 6.70 (1H, br s), 3.80 (3H, s).

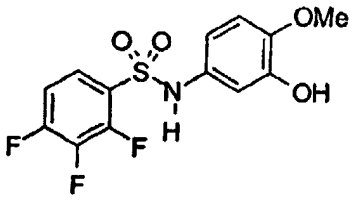
Example 16



1-[(3-Chloro-4-methoxyphenyl)aminosulfonyl]-2,3,4-trifluorobenzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2,3,4-trifluorophenylsulfonyl chloride and replacing *p*-anisidine with 3-chloro-4-methoxyaniline. ^{1}H-NMR ($CDCl_3$): ∂ 7.56 (1H, m), 7.17 (1H, d, J = 2.0 Hz), 7.02 (1H, m), 6.98 (1H, dd, J = 9.0 and 2.0 Hz), 6.78 (1H, d, J = 9.0 Hz), 6.72 (1H, br s), 3.83 (3H, s). MS(EI): 352 (7, M^+), 351 (20), 156 (100). Anal. Calcd. for $C_{13}H_9ClF_3NO_3S$: C, 44.39; H, 2.58; N, 3.98; S, 9.11. Found: C, 44.31; H, 2.58; N, 3.96; S, 9.08.

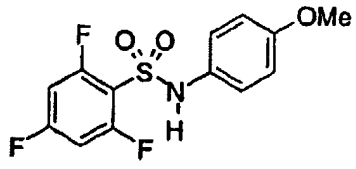
Example 17



1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2,3,4-trifluorobenzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2,3,4-trifluorophenylsulfonyl chloride and replacing *p*-anisidine with 3-hydroxy-4-methoxyaniline. ^{1}H-NMR ($CDCl_3$): ∂ 7.55 (1H, m), 7.00 (1H, m), 6.70 (2H, m), 6.60 (2H, m), 5.61 (1H, s), 3.83 (3H, s). Anal. Calcd. for $C_{13}H_{10}F_3NO_4S$: C, 46.85; H, 3.02; N, 4.20; S, 9.62. Found: C, 46.79; H, 3.03; N, 4.24; S, 9.53.

Example 18

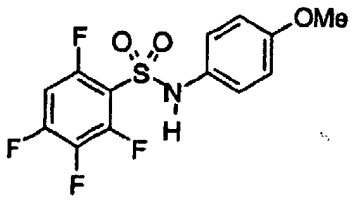


2,4,6-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 1 by replacing 4-fluoro-3-nitrophenylsulfonyl chloride with 2,4,6-trifluorophenylsulfonyl chloride

(Example C). ^{1}H-NMR ($CDCl_3$): ∂ 7.08 (2H, dd, J = 9.0 and 2.0 Hz), 6.8-6.7 (5H, m), 3.75 (3H, s). Anal. Calcd. for $C_{13}H_{10}F_3NO_3S$: C, 49.21; H, 3.18; N, 4.41; S, 10.10. Found: C, 49.13; H, 3.20; N, 4.39; S, 10.01.

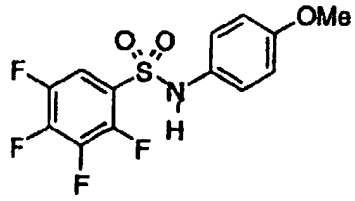
Example 19



2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene.

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzene (250 mg, 0.6 mmol) (Example 5) was dissolved in methanol (25 ml) and placed in a closed vessel. A catalytic amount of 10% Pd/charcoal (25 mg) was added and the mixture was hydrogenated at 60 psi H_2 for 4 h. The mixture was filtered through celite, the solvent was evaporated and the residue was purified by chromatography (silica; EtOAc/Hexane, 1:4) to yield 82 mg of the title compound. ^{1}H-NMR ($CDCl_3$): ∂ 7.10 (2H, dd, J = 9.0 and 2.0 Hz), 6.94 (1H, br s), 6.85 (1H, m), 6.79 (2H, dd, J = 9.0 and 2.0 Hz), 3.75 (3H, s). MS(EI): 335 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_9F_4NO_3S$: C, 46.57; H, 2.71; N, 4.18; S, 9.56. Found: C, 46.46; H, 2.67; N, 4.17; S, 9.52.

Example 20

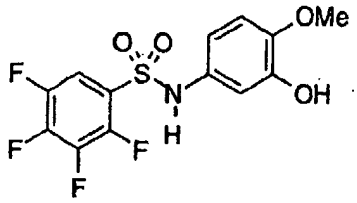


2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 19 by replacing 1-bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzene with 1-bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene (Example 4). ^{1}H-NMR ($CDCl_3$): ∂ 7.40 (1H, m), 7.05 (2H, dd, J = 9.0 and 2.0 Hz), 6.80 (2H, dd, J = 9.0 and

2.0 Hz), 3.76 (3H, s). MS(EI): 335 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_9F_4NO_3S$: C, 46.57; H, 2.71; N, 4.18; S, 9.56. Found: C, 46.44; H, 2.67; N, 4.13; S, 9.47.

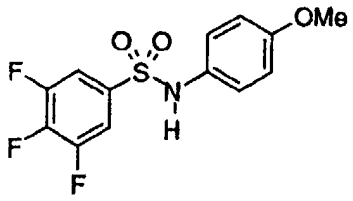
Example 21



2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 19 by replacing 1-bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzene with 1-bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene (Example 3). ^{1}H-NMR ($CDCl_3$): ∂ 7.43 (1H, m), 6.80 (1H, br s), 6.73-6.60 (3H, m), 5.67 (1H, s), 3.84 (3H, s). MS(EI): 351 (20, M^+), 138 (100). Anal. Calcd. for $C_{13}H_9F_4NO_4S$: C, 44.45; H, 2.58; N, 3.99; S, 9.13. Found: C, 44.39; H, 2.59; N, 3.94; S, 9.24.

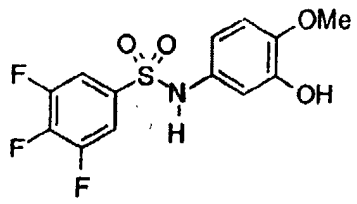
Example 22



3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 19 by replacing 1-bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzene with 1-bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene (Example 11). ^{1}H-NMR ($CDCl_3$): ∂ 7.35 (2H, t, J = 6.0 Hz), 7.00 (2H, d, J = 9.0 Hz), 6.81 (2H, d, J = 9.0 Hz), 3.78 (3H, s). MS(EI) : 317 (20, M^+), 122 (100). Anal. Calcd. for $C_{13}H_{10}F_3NO_3S$: C, 49.21; H, 3.18; N, 4.41; S, 10.10. Found: C, 49.09; H, 3.15; N, 4.37; S, 10.03.

Example 23



3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene.

The title compound was prepared in a manner similar to that described in Example 19 by replacing 1-bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzene with 1-bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene (Example 13). ^{1}H-NMR ($CDCl_3$): ∂ 7.38 (2H, t, J = 6.0 Hz), 6.74 (1H, d, J = 9.0 Hz), 6.64 (1H, d, J = 2.0 Hz), 6.58 (1H, dd, J = 9.0 and 2.0 Hz), 5.64 (1H, s), 3.88 (3H, s). Anal. Calcd. for $C_{13}H_{10}F_3NO_4S$: C, 46.85; H, 3.02; N, 4.20; S, 9.62. Found: C, 46.75; H, 3.01; N, 4.20; S, 9.56.

Example 24

Assessment of Biological Activity.

Compounds were evaluated for their ability to inhibit *in vitro* the growth of HeLa cells, an immortal cell line derived from a human cervical carcinoma commonly used to evaluate the cytotoxicity of potential therapeutic agents. The following data reflect the cytotoxicity of selected examples of the present invention. The values given represent the concentration of test compound required to inhibit by 50% the uptake of Alamar Blue (Biosource International, Camarillo, CA) by HelA cell cultures, which correlates directly with the overall levels of cellular metabolism in the culture, and is generally accepted as an appropriate marker of cell growth. The test was conducted according to the method of Ahmed et al. (*J. Immunol. Methods* **1994**, *170*, 211). The following selected examples display potent cytotoxic activity in this assay, with IC_{50} values ranging from 0.05 μM to 5.0 μM.

Compound	IC50 (μM)
Example 2	0.15

Example 3	0.05
Example 4	0.15
Example 5	0.15
Example 6	5.0
Example 7	1.5
Example 8	0.15
Example 9	0.05
Example 10	0.5
Example 11	0.5
Example 17	1.5
Example 19	5.0
Example 20	0.5
Example 21	0.15
Example 22	5.0
Example 23	1.5

Certain compounds were evaluated for their ability to increase LDL receptor expression in HepG2 cells using western-blot analysis as described by Tam et al., (*J. Biol. Chem.*, **1991**, *266*, 16764). The data presented (EC_{max}) reflect the minimum concentration at which a maximal induction of LDL receptor levels was observed for each compound. In all cases, the level of induction was greater than that observed under lipid-free conditions (activated system) in the absence of the test compounds.

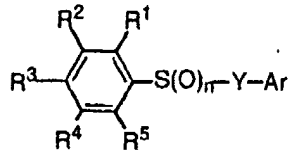
Compound	EC_{max} (μm)
Example 1	5
Example 2	1.5
Example 3	0.15
Example 4	0.5
Example 5	0.5
Example 6	50

Example 7	50
Example 8	0.5
Example 9	0.15
Example 10	1.5
Example 11	1.5
Example 19	15
Example 20	1.5
Example 21	0.5
Example 22	5

All publications and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference. Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily apparent to those of ordinary skill in the art in light of the teachings of this invention that certain changes and modifications may be made thereto without departing from the spirit or scope of the appended claims.

WHAT IS CLAIMED IS:

1. A compound having the Formula I:



or a pharmaceutically acceptable salt thereof, wherein:

the subscript n is 1 or 2;

R^1, R^2, R^4, and R^5 are independently selected from hydrogen, lower alkyl, halogen, OCF_3, CF_3, NO_2, CO_2H, CN, SO_2-$N(R^6)(R^7)$, SO_2-R^8, CO_2-R^8, and CO-R^8;

R^3 is a leaving group;

Y is a single bond, -O-, -$N(R^9)$-, -$N(R^9)$-CH_2-, or -$CH(R^9)$-;

and Ar is an optionally substituted aryl or heteroaryl group;

wherein R^6 and R^7 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl; R^8 is selected from lower alkyl or lower heteroalkyl; and R^9 is selected from:

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

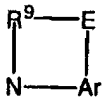
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein, if Y is -N(R^9)-, then R^9 and Ar may be connected by a linking group E to give a substituent of the Formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^9, E, Ar and the nitrogen atom contains no more than 8 atoms, or preferably R^9 and Ar may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom;

with the following provisos:

• At least one of the R^1, R^2, R^4, and R^5 groups is other than hydrogen or lower alkyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = F$, then Y is a single bond or -CH(R^9)-;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Cl$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl or unsubstituted *p*-biphenyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Br$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl;

• When R^3 = halogen, n = 2, Y = -N(R^9)-, and at least one of R^1, R^2, R^4 and R^5 is also halogen, then at least one of R^1, R^2, R^4 and R^5 must be other than hydrogen;

• When R^1 = H, n = 2, and Y = -NH-, then at least one of R^2, R^3, R^4 and R^5 must be a substituent other than chloro;

• When R^1 = R^5 = H, n = 2, and Y = -N(R^9)-, then at least one of R^2, R^3, and R^4 must be a substituent other than chloro;

• When R^1 = R^5 = halogen, R^2 = R^4 = H, n = 2, and Y = -N(R^9)-, then R^3 is a substituent other than chloro or bromo;

• When R^1 = R^2 = halogen, R^4 = R^5 = H, n = 2, and Y = -N(R^8)-, then R^3 is a substituent other than chloro or bromo;

• When R^1 = R^4 = halogen, R^2 = R^5 = H, and n = 2, then R^3 is a substituent other than chloro or bromo;

• When R^1 = R^5 = halogen, R^2 = R^4 = H, and Y = -O-, then Ar is a ring system other than quinolinyl;

• When R^1 = F, R^3 = R^4 = Cl, and Y = -NH-, then Ar is a ring system other than 1,3,4-thiadiazolyl;

• When R^1 = R^3 = F, R^4 = Cl, and Y = -NH- or -O-, then Ar is a ring other than unsubstituted phenyl;

• When R^1 = R^3 = R^5 = Br, and Y = -NH-, then Ar is a ring other than phenyl substituted by lower-alkyl;

• When R^1 = R^3 = R^5 = Cl, Y = -NH-, and R^9 = H or methyl, then Ar is a phenyl ring substituted by 1-4 groups chosen independently from halogen, OH, OR', NH_2, NHR', and NR'R";

• When R^2 = R^3 = R^4 = Cl, Y = -NH-, and R^9 = propargyl, then Ar is an unsubstituted ring or a ring substituted by a group other than a trifluoromethyl or nitro groups;

•When R^1 = R^3 = Cl and Y = -N(R^9)-, then R^2 and R^4 must both be other than chloro;

• When R^2 = CF_3, R^3 = Cl, and Y = -N(R^9)-, then Ar cannot be either a phenyl ring substituted by trifluoromethyl, nitro, chloro, or lower-alkyl groups, or a 2-benzothiazolyl ring;

• When R^2 = CO_2H or NO_2, R^3 = Cl, and Y = -N(R^9)-, then Ar is an unsubstituted phenyl or phenyl substituted by a substituent other than CO_2H or CO_2-R';

• When $R^1 = NO_2$, R^3 = Cl, and Y = -NH-, then Ar is a ring system other than phenyl substituted by either Br or NO_2;

wherein R' and R" are independently chosen from the group of C1-C8 alkyl groups; and wherein said compound has pharmacological activity.

2. The compound of claim 1, wherein R^3 is halogen, NO_2, OCF_3, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-(R^8), N(R^6)-SO_2-Ar, N(R^6)-CO-(R^8), N(R^6)-CO-Ar, N[CO-R^8]$_2$, N(R^8)$_3^+$, N(R^8)$_2$(Ar)$^+$, O-SO_2-Ar, O-SO_2-R^8, O-CO-R^8, O-CO-Ar, O-Ar, O-R^8, or O-CO-CF_3.

3. The compound of claim 2, wherein n = 2.

4. The compound of claim 3, wherein R^1, R^2, R^4 and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, SO_2-R^8, NO_2, CN, CO_2-R^8, and SO_2-N(R^6)(R^7).

5. The compound of claim 4, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

6. The compound of claim 5, wherein Y is a single bond, -N(R^9)-, or -CH(R^9)-; and wherein R^6, R^7 and R^9 are independently chosen from hydrogen, lower-alkyl and lower-heteroalkyl.

7. The compound of claim 6, wherein Y is -N(R^9)-.

8. The compound of claim 7, wherein R^3 is halogen, OCF_3, NO_2, N_3, O-SO_2-Ar, O-SO_2-R^8, or SO_2-Ar.

9. The compound of claim 8, wherein R^3 is F, Cl, Br, or OCF_3.

10. The compound of claim 9, wherein R^3 is F.

11. The compound of claim 10, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

12. The compound of claim 11, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-fluorobenzonitrile;

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester.

13. The compound of claim 12, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene; or

4-Fluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

14. The compound of claim 12, wherein the compound is:

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

15. The compound of claim 10, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

16. The compound of claim 15, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2- [(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene; or

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene.

17. The compound of claim 16, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

-1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene; or

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene.

18. The compound of claim 16, wherein the compound is:

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene; or

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene.

19. The compound of claim 9, wherein R^3 is Cl.

20. The compound of claim 19, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

21. The compound of claim 20, wherein the compound is:

1-Chloro-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester.

22. The compound of claim 19, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

23. The compound of claim 22, wherein the compound is:

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

1-Chloro-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

24. The compound of claim 9, wherein R^3 is Br.

25. The compound of claim 24, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

26. The compound of claim 25, wherein the compound is:

1-Bromo-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester.

27. The compound of claim 24, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

28. The compound of claim 27, wherein the compound is:

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

1-Bromo-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

29. The compound of claim 9, wherein R^3 is OCF_3.

30. The compound of claim 29, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

31. The compound of claim 30, wherein the compound is:

4-Trifluoromethoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester.

32. The compound of claim 29, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

33. The compound of claim 32, wherein the compound is:

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

34. The compound of claim 8, wherein R^3 is selected from NO_2, N_3, O-SO_2-Ar, O-SO_2-R^8 and SO_2-Ar.

35. The compound of claim 34, wherein the compound is:

1-[(4-Methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Azido-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile.

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester.

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-4-nitrobenzene;

4-Azido-2,3,6-trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

4-Azido-2,3,6-trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

36. The compound of claim 7, wherein R^3 is selected from $N(R^6)$-SO_2-CF_3, $N(R^6)$-SO_2-(R^8), $N(R^6)$-SO_2-Ar, $N(R^6)$-CO-(R^8), $N(R^6)$-CO-Ar, $N[CO\text{-}R^8]_2$, and O-CO-CF_3.

37. The compound of claim 36, wherein the compound is:

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethylsulfonamido-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethyl-sulfonamidobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-aminosulfonyl]benzene;

4-(Diacetylamino)-2,3-difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-5-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene; or

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamido-benzene.

38. The compound of claim 6, wherein Y is a single bond or -CH(R^9)-.

39. The compound of claim 38, wherein R^3 is selected from F, Cl, Br, and OCF_3.

40. The compound of claim 39, wherein R^2 is selected from NO_2, CN, and CO_2R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

41. The compound of claim 40, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

1-Chloro-4-[(4-methoxyphenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-methoxyphenyl)sulfonyl]-2-nitrobenzene; or

1-Chloro-4-[(4-dimethylaminophenyl)sulfonyl]-2-nitrobenzene.

42. The compound of claim 39, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

43. The compound of claim 42, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)sulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)methylsulfonyl]benzene; or

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)methylsulfonyl]benzene.

44. The compound of claim 38, wherein R^3 is selected from NO_2, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-(R^8), N(R^6)-SO_2-Ar, N(R^6)-CO-(R^8), N(R^6)-CO-Ar, N[CO-

$R^8]_2$, $N(R^8)_3^+$, $N(R^8)_2(Ar)^+$, $O\text{-}SO_2\text{-}Ar$, $O\text{-}SO_2\text{-}R^8$, $O\text{-}CO\text{-}R^8$, O-CO-Ar, O-Ar, $O\text{-}R^8$ and O-$CO\text{-}CF_3$.

45. The compound of claim 44, wherein R^2 is selected from NO_2, CN, and $CO_2\text{-}R^8$; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and $CO_2\text{-}R^8$.

46. The compound of claim 45, wherein the compound is:

1-[(4-Methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile.

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene; or

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene.

47. The compound of claim 44, wherein R^2 and R^4 are independently selected from hydrogen, F, Ci, Br, OCF_3 and CF_3.

48. The compound of claim 47, wherein the compound is:

2,3,5,6-Tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene; or

4-Azido-2,3,5,6-tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene.

49. The compound of claim 2, wherein n = 1

50. The compound of claim 49, wherein the compound is:

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulfenyl]benzene;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)sulfenyl]benzoic acid, ethyl ester;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfenyl]benzonitrile;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfenyl]benzene;

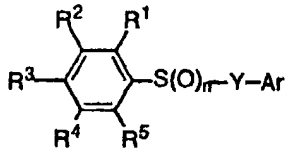
2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfenyl]benzene; or

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfenyl]benzene.

51. A pharmaceutical composition comprising a pharmaccutically acceptable excipient and a compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

the subscript n is 1 or 2;

R^1, R^2, R^4, and R^5 are independently selected from hydrogen, lower alkyl, halogen, OCF_3, CF_3, NO_2, CO_2H, CN, SO_2-$N(R^6)(R^7)$, SO_2-R^8, CO_2-R^8, and CO-R^8;

R^3 is a leaving group;

Y is a single bond, -O-, -$N(R^9)$-, -$N(R^9)$-CH_2-, or -$CH(R^9)$-;

and Ar is an optionally substituted aryl or heteroaryl group;

wherein R^6 and R^7 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl; R^8 is selected from lower alkyl or lower heteroalkyl; and R^9 is selected from:

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

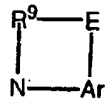
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein, if Y is -N(R^9)-, then R^9 and Ar may be connected by a linking group E to give a substituent of the Formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^9, E, Ar and the nitrogen atom contains no more than 8 atoms, or preferably R^9 and Ar may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom;

with the following provisos:

• At least one of the R^1, R^2, R^4, and R^5 groups is other than hydrogen or lower alkyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = F$, then Y is a single bond or -CH(R^9)-;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Cl$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl or unsubstituted *p*-biphenyl;

• When $R^1 = R^2 = R^3 = R^4 = R^5 = Br$, n = 2, and Y = -NH-, then Ar is other than unsubstituted phenyl;

• When R^3 = halogen, n = 2, Y = -N(R^9)-, and at least one of R^1, R^2, R^4 and R^5 is also halogen, then at least one of R^1, R^2, R^4 and R^5 must be other than hydrogen;

• When R^1 = H, n = 2, and Y = -NH-, then at least one of R^2, R^3, R^4 and R^5 must be other than chloro;

• When $R^1 = R^5$ = H, n = 2, and Y = -N(R^9)-, then at least one of R^2, R^3, and R^4 must be a substituent other than chloro;

• When $R^1 = R^3 = R^5 = Cl$, Y = -NH-, and R^9 = H or methyl, then Ar is a phenyl ring substituted by 1-4 groups chosen independently from halogen, OH, OR', NH_2, NHR', and NR'R";

•When $R^1 = R^3$ = Cl and Y = -N(R^9)-, then R^2 and R^4 must both be other than chloro; and

• When $R^2 = CF_3$, R^3 = Cl, and Y = -N(R^9)-, then Ar cannot be either a phenyl ring substituted by trifluoromethyl, nitro, chloro, or lower-alkyl groups, or a 2-benzothiazolyl ring.;

wherein said compound has pharmacological activity.

52. The composition of claim 51, wherein R^3 is halogen, NO_2, OCF_3, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-R^8, N(R^6)-SO_2-Ar, N(R^6)-CO-(R^8), N(R^6)-CO-Ar, N[CO-R^8]$_2$, N(R^8)$_3^+$, N(R^8)$_2$(Ar)$^+$, O-SO_2-Ar, O-SO_2-R^8, O-CO-R^8, O-CO-Ar, O-Ar, O-R^8, or O-CO-CF_3.

53. The composition of claim 52, wherein n = 2, and R^1, R^2, R^4 and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, , SO_2-R^8, NO_2, CN, CO_2-R^8, and SO_2-N(R^6)(R^7).

54. The composition of claim 53, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

55. The composition of claim 54, wherein Y is -N(R^9)-, and R^6, R^7 and R^9 are independently chosen from hydrogen, lower alkyl and lower heteroalkyl.

56. The composition of claim 55, wherein R^3 is halogen, OCF_3, NO_2, N_3, O-SO_2-Ar, O-SO_2-R^8, or SO_2-Ar.

57. The composition of claim 56, wherein R^3 is F, Cl, Br, or OCF_3.

58. The composition of claim 57, wherein R^3 is F.

59. The composition of claim 58, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

60. The composition of claim 59, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2,4,5,6-Tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester.

61. The composition of claim 60, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene; or

4-Fluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

62. The composition of claim 58, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

63. The composition of claim 62, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2- [(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene; or

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene.

64. The composition of claim 63, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene; or

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

65. The composition of claim 63, wherein the compound is:

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene; or

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

66. The composition of claim 57, wherein R^3 is Cl; R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

67. The composition of claim 66, wherein the compound is:

1-Chloro-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile; or

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile.

68. The composition of claim 57, wherein R^3 is Cl; and R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

69. The composition of claim 68, wherein the compound is:

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

1-Chloro-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

70. The composition of claim 57, wherein R^3 is Br; R^2 is selected from NO_2, CN, and CO_2-R^8 and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

71. The composition of claim 70, wherein the compound is:

1-Bromo-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1- Bromo -4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1- Bromo -4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1- Bromo -4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1- Bromo -4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2- Bromo -5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2- Bromo -5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2- Bromo -5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2- Bromo -5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile; or

2- Bromo -5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile.

72. The composition of claim 57, wherein R^3 is Br; and R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

73. The composition of claim 72, wherein the compound is:

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1- Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1- Bromo-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

1- Bromo-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

74. The composition of claim 57, wherein R^3 is OCF_3; R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

75. The composition of claim 74, wherein the compound is:

4-Trifluoromethoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester; or

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester.

76. The composition of claim 57, wherein R^3 is OCF_3; and R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

77. The composition of claim 76, wherein the compound is:

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

78. The composition of claim 56, wherein R^3 is selected from NO_2, N_3, $O\text{-}SO_2\text{-}Ar$, $O\text{-}SO_2\text{-}R^8$ and $SO_2\text{-}Ar$.

79. The composition of claim 78, wherein the compound is:

1-[(4-Methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Azido-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile.

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester.

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-4-nitrobenzene;

4-Azido-2,3,6-trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

4-Azido-2,3,6-trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

80. The composition of claim 55, wherein R^3 is selected from $N(R^6)$-SO_2-CF_3, $N(R^6)$-SO_2-R^8, $N(R^6)$-SO_2-Ar, $N(R^6)$-CO-R^8, $N(R^6)$-CO-Ar, $N[CO\text{-}R^8]_2$, or O-CO-CF_3.

81. The composition of claim 80, wherein the compound is:

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethylsulfonamido-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethyl-sulfonamidobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-aminosulfonyl]benzene;

4-(Diacetylamino)-2,3-difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-5-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene; or

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamido-benzene.

82. The composition of claim 54, wherein Y is a single bond or $-CH(R^9)-$.

83. The composition of claim 82, wherein R^3 is selected from F, Cl, Br, and OCF_3.

84. The composition of claim 83, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

85. The composition of claim 84, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

1-Chloro-4-[(4-methoxyphenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-methoxyphenyl)sulfonyl]-2-nitrobenzene; or

1-Chloro-4-[(4-dimethylaminophenyl)sulfonyl]-2-nitrobenzene;

86. The composition of claim 83, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

87. The composition of claim 86, wherein the compound is:

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)sulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)methylsulfonyl]benzene; or

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)methylsulfonyl]benzene.

88. The composition of claim 82, wherein R^3 is selected from NO_2, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-R^8, N(R^6)-SO_2-Ar, N(R^6)-CO-R^8, N(R^6)-CO-Ar, N[CO-R^8]$_2$, N(R^8)$_3^+$, N(R^8)$_2$(Ar)$^+$, O-SO_2-Ar, O-SO_2-R^8, O-CO-R^8, O-CO-Ar, O-Ar, O-R^8, and O-CO-CF_3.

89. The composition of claim 88, wherein R^2 is selected from NO_2, CN, and CO_2-R^8; and R^4 is selected from hydrogen, F, Cl, Br, OCF_3, CF_3, NO_2, CN, and CO_2-R^8.

90. The composition of claim 89, wherein the compound is:

1-[(4-Methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile.

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene; or

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene.

91. The composition of claim 88, wherein R^2 and R^4 are independently selected from hydrogen, F, Cl, Br, OCF_3 and CF_3.

92. The composition of claim 91, wherein the compound is:

2,3,5,6-Tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene; or

4-Azido-2,3,5,6-tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene.

93. The composition of claim 52, wherein n = 1.

94. The composition of claim 93, wherein the compound is:

3-Bromo-2,4,5,6-tetrafluoro-1-[(4-methoxyphenyl)sulfenyl]benzene;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)sulfenyl]benzoic acid, ethyl ester;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfenyl]benzonitrile;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfenyl]benzene;

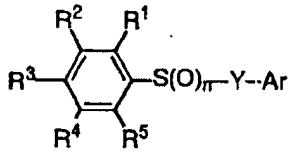
2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfenyl]benzene; or

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfenyl]benzene.

95. A method of treating or preventing a disease state characterized by abnormally high levels of low density lipoprotein particles or cholesterol in the blood, or by an abnormally high level of cell proliferation, which method comprises administering to a mammalian subject in need thereof a therapeutically effective amount of a composition containing a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

the subscript n is 1 or 2;

R^1, R^2, R^4, and R^5 are independently selected from hydrogen, lower alkyl, halogen, OCF_3, CF_3, NO_2, CO_2H, CN, SO_2-$N(R^6)(R^7)$, SO_2-R^8, CO_2-R^8, and CO-R^8;

R^3 is a leaving group;

Y is a single bond, -O-, -$N(R^9)$-, -$N(R^9)$-CH_2-, or -$CH(R^9)$-;

and Ar is an optionally substituted aryl or heteroaryl group;

wherein R^6 and R^7 are independently chosen from hydrogen, lower alkyl, and lower heteroalkyl; R^8 is selected from lower alkyl or lower heteroalkyl; and R^9 is selected from:

hydrogen,

substituted or unsubstituted (C1-C10)alkyl,

substituted or unsubstituted (C1-C10)alkoxy,

substituted or unsubstituted (C3-C6)alkenyl,

substituted or unsubstituted (C2-C6)heteroalkyl,

substituted or unsubstituted (C3-C6)heteroalkenyl,

substituted or unsubstituted (C3-C6)alkynyl,

substituted or unsubstituted (C3-C8)cycloalkyl,

substituted or unsubstituted (C5-C7)cycloalkenyl,

substituted or unsubstituted (C5-C7)cycloalkadienyl,

substituted or unsubstituted aryl,

substituted or unsubstituted aryloxy,

substituted or unsubstituted aryl-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C5-C7)cycloalkenyl,

substituted or unsubstituted aryloxy-(C3-C8)cycloalkyl,

substituted or unsubstituted aryl-(C1-C4)alkyl,

substituted or unsubstituted aryl-(C1-C4)alkoxy,

substituted or unsubstituted aryl-(C1-C4)heteroalkyl,

substituted or unsubstituted aryl-(C3-C6)alkenyl,

substituted or unsubstituted aryloxy-(C1-C4)alkyl,

substituted or unsubstituted aryloxy-(C2-C4)heteroalkyl,

substituted or unsubstituted heteroaryl,

substituted or unsubstituted heteroaryloxy,

substituted or unsubstituted heteroaryl-(C1-C4)alkyl,

substituted or unsubstituted heteroaryl-(C1-C4)alkoxy,

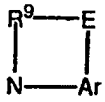
substituted or unsubstituted heteroaryl-(C1-C4)heteroalkyl,

substituted or unsubstituted heteroaryl-(C3-C6)alkenyl,

substituted or unsubstituted heteroaryloxy-(C1-C4)alkyl, and

substituted or unsubstituted heteroaryloxy-(C2-C4)heteroalkyl,

wherein, if Y is -N(R^9)-, then R^9 and Ar may be connected by a linking group E to give a substituent of the Formula



wherein E represents a bond, (C1-C4) alkylene, or (C1-C4) heteroalkylene, and the ring formed by R^9, E, Ar and the nitrogen atom contains no more than 8 atoms, or preferably R^9 and Ar may be covalently joined in a moiety that forms a 5- or 6-membered heterocyclic ring with the nitrogen atom.

96. The method of claim 95, wherein R^3 is halogen, NO_2, OCF_3, S(O)-Ar, SO_2-R^8, SO_2-Ar, N_3, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-R^8, N(R^6)-SO_2-Ar, N(R^6)-CO-(R^8), N(R^6)-CO-Ar, N[CO-R^8]$_2$,

$N(R^8)_3^+$, $N(R^8)_2(Ar)^+$, O-SO_2-Ar, O-SO_2-R^8, O-CO-R^8, O-CO-Ar, O-Ar, O-R^8, or O-CO-CF_3.

97. The method of claim 96, wherein n = 2, and R^1, R^2, R^4 and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, SO_2-R^8, NO_2, CN, CO_2-R^8, and SO_2-N(R^6)(R^7).

98. The method of claim 97, wherein Y is -N(R^9)-, and wherein R^6, R^7 and R^9 are independently chosen from hydrogen, lower-alkyl and lower-heteroalkyl.

99. The method of claim 98, wherein R^3 is halogen or OCF_3.

100. The method of claim 99, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Fluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-fluorobenzonitrile;

4,5-Difluoro-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4,5-Difluoro-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)aminosulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)aminosulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2- [(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,4-trifluoro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-3,4,5-trifluoro-2-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,6-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Chloro-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Chloro-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Chloro-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-4-[(4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(3,4-dimethoxyphenyl)aminosulfonyl]-2-nitrobenzene;

1-Bromo-4-[(4-dimethylaminophenyl)aminosulfonyl]-2-nitrobenzene;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Bromo-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Bromo-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

1-Bromo-2,3,6-trifluoro-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

4-Trifluoromethoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoromethoxy-1-[(4-dimethylaminophenyl)aminosulfonyl]-3-nitrobenzene;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

2-Trifluoromethoxy-5-[(4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzoic acid, ethyl ester;

2-Trifluoromethoxy-5-[(4-dimethylaminophenyl)aminosulfonyl]benzoic acid, ethyl ester;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

2,3,6-Trifluoro-1-trifluoromethoxy-4-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

101. The method of claim 98, wherein R^3 is selected from NO_2, N_3, O-SO_2-Ar, O-SO_2-R^8 and SO_2-Ar.

102. The method of claim 101, wherein the compound is:

1-[(4-Methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzonitrile.

2-Azido-5-[(3,4-dimethoxyphenyl)aminosulfonyl]benzonitrile;

2-Azido-5-[(4-dimethylaminophenyl)aminosulfonyl]benzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile.

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonylbenzonitrile;

5-[(4-Methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(3,4-Dimethoxyphenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester;

5-[(4-Dimethylaminophenyl)aminosulfonyl]-2-phenylsulfonyloxybenzoic acid, ethyl ester.

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]-4-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]-4-nitrobenzene;

4-Azido-2,3,6-trifluoro-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

4-Azido-2,3,6-trifluoro-1-[(4-dimethylaminophenyl)aminosulfonyl]benzene; or

4-Azido-2,3,6-trifluoro-1-[(3,4-dimethoxyphenyl)aminosulfonyl]benzene.

103. The method of claim 98, wherein R^3 is selected from $N(R^6)$-SO_2-CF_3, $N(R^6)$-SO_2-R^8, $N(R^6)$-SO_2-Ar, $N(R^6)$-CO-R^8, $N(R^6)$-CO-Ar, $N[CO\text{-}R^8]_2$, or O-CO-CF_3.

104. The method of claim 103, wherein the compound is:

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethylsulfonamido-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-trifluoromethyl-sulfonamidobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-aminosulfonyl]benzene;

4-(Diacetylamino)-2,3-difluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-5-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-3-nitrobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-methylsulfonamido-benzene;

1-[(4-Methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Fluoro-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)aminosulfonyl]-3-nitro-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamidobenzene; or

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)aminosulfonyl]-4-phenylsulfonamido-benzene.

105. The method of claim 97, wherein Y is a single bond or -CH(R^9)-; and R^3 is halogen, OCF_3, NO_2, N_3, O-SO_2-Ar, O-SO_2-R^8, or SO_2-Ar.

106. The method of claim 105, wherein the compound is:

4-Fluoro-1-[(4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Fluoro-5-[(4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2-Fluoro-5-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzonitrile;

2,3,4-Trifluoro-5-[(4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

2,3,4-Trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzoic acid, ethyl ester;

1-Chloro-4-[(4-methoxyphenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)methylsulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-methoxyphenyl)sulfonyl]-2-nitrobenzene;

1-Chloro-4-[(4-dimethylaminophenyl)sulfonyl]-2-nitrobenzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-3,4,5,6-tetrafluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulfonyl)]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,4,5,6-tetrafluoro-3-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(4-methoxyphenyl)sulfony]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-4,5,6-trifluoro-2-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5-Tetrafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

3,4,5-Trifluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Chloro-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(4-dimethylaminophenyl)sulfonyl]benzene;

1-Bromo-2,3,5,6-tetrafluoro-4-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)methylsulfonyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)methylsulfonyl]benzene;

1-[(4-Methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile.

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene; or

4-Azido-2,3,5,6-tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene.

107. The method of claim 97, wherein Y is a single bond or -CH(R^9)-; and R^3 is selected from S(O)-Ar, SO_2-R^8, N(R^6)-SO_2-CF_3, N(R^6)-SO_2-R^8, N(R^6)-SO_2-Ar, N(R^6)-CO-R^8, N(R^6)-CO-Ar, N[CO-R^8]$_2$, N(R^8)$_3^+$, N(R^8)$_2$(Ar)$^+$, O-CO-R^8, O-CO-Ar, O-Ar, O-R^8, and O-CO-CF_3.

108. The method of claim 107, wherein the compound is:

1-[(4-Methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-3,4-dinitrobenzene;

4-Azido-1-[(3,4-dimethoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-aminophenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Azido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

2-Azido-5-[(4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzonitrile;

2-Azido-5-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzonitrile.

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyl)benzonitrile;

5-[(4-Methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

5-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-2-(phenylsulfonyloxy)benzoic acid, ethyl ester;

4-Trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

4-Trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-methylsulfonamido-3-nitrobenzene;

1-[(4-Methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Fluoro-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

1-[(3-Hydroxy-4-methoxyphenyl)sulfonyl]-4-phenylsulfonamido-3-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-[(3-fluoro-4-methoxyphenyl)sulfonyl]-1-nitrobenzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-fluoro-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoromethylsulfonamido-1-[(3-hydroxy-4-methoxyphenyl)-sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-4-trifluoroacetoxy-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(methylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

2,3,5,6-Tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]-4-(phenylsulfonamido)benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(4-methoxyphenyl)sulfonyl]benzene;

4-Azido-2,3,5,6-tetrafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfonyl]benzene; or

4-Azido-2,3,5,6-tetrafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfonyl]benzene.

109. The method of claim 96, wherein n = 1, and R^1, R^2, R^4 and R^5 are independently selected from hydrogen, F, Cl, Br, OCF_3, CF_3, SO_2-R^8, NO_2, CN, CO_2-R^8, and SO_2-$N(R^6)(R^7)$.

110. The method of claim 109, wherein the compound is:

1-Bromo-2,4,5,6-tetrafluoro-3-[(4-methoxyphenyl)sulfenyl]benzene;

2,4,5,6-Tetrafluoro-3-[(4-dimethylaminophenyl)sulfenyl]benzoic acid, ethyl ester;

4-Fluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]-3-nitrobenzene;

2-Fluoro-5-[(4-methoxyphenyl)sulfenyl]benzonitrile;

1,3-Dichloro-2,4,6-trifluoro-5-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-hydroxy-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(3-fluoro-4-methoxyphenyl)sulfenyl]benzene;

2,3,4,5,6-Pentafluoro-1-[(4-dimethylaminophenyl)sulfenyl]benzene; or

2,3,4,5,6-Pentafluoro-1-[(3,4-dimethoxyphenyl)sulfenyl]benzene.

111. The method of claim 95, wherein the composition is administered in combination with a therapeutically effective amount of a hypolipidemic agent or a hypocholesterolemic agent that is not represented by Formula I.

112. The method of claim 95, wherein the composition is administered in combination with a therapeutically effective amount of an antineoproliferative, chemotherapeutic, or cytotoxic agent that is not represented by formula I.

113. The method of claim 95, wherein the compound is administered as a prodrug.

114. The method of claim 95, wherein the compound is conjugated to a targeting molecule which preferentially directs the compound to a targeted cell.

115. The method of claim 95, wherein the disease state is cancer or a cancerous condition.

116. The method of claim 95, wherein the proliferative disease state is infection by a microorganism.

117. The method of claim 95, wherein the proliferative disease state is psoriasis.

118. The method of claim 95, wherein the proliferative disease state is vascular restenosis.

119. The method of claim 95, wherein the disease state is hypercholesterolemia or another disease state associate with abnormally high blood levels of cholesterol or lipoproteins.

120. The method of claim 95, wherein the composition is administered orally.

121. The method of claim 95, wherein the composition is administered intravenously or intramuscularly.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/16781

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07C311/21 A61K31/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07C A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 143 937 A (H.-J. LANG, ET AL.) 1 September 1992 see columns 1-4; examples 1,2,12,18,19,21, 31,35,39,40,45 ---	1-9,19, 51-57, 95-99, 119
X	DE 622 494 C (I.G. FARBENINDUSTRIE) 29 November 1935 see examples 1-4,6-8,12,15 ---	1-6,38, 44
X	US 2 358 365 A (B.F. TULLAR) 19 September 1944 see page 2, right-hand column, line 3 - line 15 ---	1-6,38, 44
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

' Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 November 1998	27/11/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	English, R

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 859 345 A (J.R. GEIGY) 18 January 1961 see page 1; claims 1-3; examples 1,3	1-9,19, 22
X	GB 938 890 A (BOOTS PURE DRUG) 9 October 1963 see page 1; claims 1,2; tables I,II,V	1-6,38, 44,47,49
X	CHEMICAL ABSTRACTS, vol. 50, no. 1, 10 January 1956 Columbus, Ohio, US; abstract no. 217g, V.O. LUKASHEVICH: "Sulphonation of halogen-substituted benzene derivatives. Formation of anhydrides of corresponding sulphonic acids" column 217; XP002083056 see abstract & DOKLADY AKAD. NAUK S.S.S.R., vol. 99, 1954, pages 995-998,	1-9,19, 22,24,27
X	GB 1 189 720 A (CIBA) 29 April 1970 see page 1; examples	1-10,19, 24
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X	I.C. POPOFF, ET AL.: "Antimalarial agents. 8. Ring-substituted bis-(4-aminophenyl) sulphones and their precursors" JOURNAL OF MEDICINAL CHEMISTRY, vol. 14, no. 12, December 1971, pages 1166-1169, XP002083052 Washington, DC, US see compounds V,VIII,X,XI,XIII,XVII,XIX, XXVIII,XXXII,XXXVI-XXXVIII,XLI,XLII,XLIV, XLV	1-6, 38-40, 42,44, 45,47
X	GB 1 306 564 A (MINNESOTA MINING & MFG) 14 February 1973 see page 12, line 33 - page 14, line 12	1-6,38, 44,47,49

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 98/16781

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	G.E. CHIVERS, ET AL.: "Studies in the chemistry of polyhalogenobenzene compounds. The synthesis and reactivity of 2,3,5,6- and 2,3,4,5-tetrachlorobenzenesulphonyl chlorides and related compounds" AUSTRALIAN JOURNAL OF CHEMISTRY, vol. 29, no. 7, July 1976, pages 1572-1582, XP002083174 Melbourne, AU see page 1579, line 36 - line 41 ---	1-9,19, 22
X	P.G. DE BENEDETTI, ET AL.: "Quantitative structure-activity analysis in dihydropteroate synthase inhibition by sulphones. Comparison with sulphanilamides" JOURNAL OF MEDICINAL CHEMISTRY, vol. 30, no. 3, March 1987, pages 459-464, XP002083053 Washington, DC, US see compounds 26,27,34 ---	1-6, 38-40, 42,44,45
X	V.N. BABUSHKIN, ET AL.: "Influence of substituents on the frequency of stretching vibrations of sulphur-containing bridging groups in diphenyl systems" JOURNAL OF GENERAL CHEMISTRY OF THE USSR, vol. 58, no. 7, pt. 2, July 1988, pages 1457-1460, XP002083054 New York, US see table 1 -----	1,2,49

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/ 16781

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 95-121
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 95-121 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: not applicable
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: not applicable

The search revealed such a large number of particularly relevant documents, in particular with regard to novelty, that the drafting of a comprehensive International Search Report is not feasible. The cited documents are considered as forming a representative sample of the revealed documents, duly taking into account their relevance with respect to the subject-matter as illustrated by the examples.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In. ational Application No
PCT/US 98/16781

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Information on patent family members

Ir. ational Application No
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